Routes toward biomimetic polysiloxanes

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Routes Toward Biomimetic Polysiloxanes

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Abstract

The synthesis and characterisation of various model compounds leading towards the formation of siloxane polymers containing pendant DNA bases has been undertaken.

Chapter 2 describes the structural characterisation of the known compounds *bis*-(trimethylsilyl)thymine (**1**), *bis*-(trimethylsilyl)cytosine (**2**), *bis*-(trimethylsilyl)adenine (**3**) and *tris*-(trimethylsilyl)guanine (**4**), synthesised by protection of the DNA base in question with HMDS in the presence of ammonium sulphate.

Chapter 3 describes the substitution of compounds **1-3** with ω-bromoalkenes. **1** reacts with allyl bromide, 4-bromo-1-butene and 5-bromo-1-pentene to form the known compound 1-allylthymine (**5**), and the poorly characterised 1-butenylthymine (**6**) and 1-pentenylthymine (**7**) respectively. **5** reacts with HMDS and ammonium sulphate to form the protected species trimethylsilyl-1-allylthymine (**11**). **6** can be similarly protected and subsequently undergoes hydrosilylation with phenyldimethylsilane to form 4-(phenyldimethylsilyl)-1-butylthymine (**12**). **12** co-crystallises with nickel-*bis*-dithiobiuret to form a metal complex interacting with thymine *via* donor-acceptor-donor hydrogen bonding interactions. **2** reacts with allyl bromide to form 1,3-*bis*-allylcytosine bromide (**8**). **3** reacts with allyl bromide and 4-bromo-1-butene to form 7,9-*bis*-allyladenine bromide hydrate (**9**) and 3-butenyladenine bromide (**10**) respectively. **8-13** have been structurally characterised.

Chapter 4 describes the formation of compounds analogous to **12** with other DNA bases, and the formation of bromobutylsiloxane compounds for subsequent reactions. 4-bromo-1-butene can be hydrosilylated with phenyldimethylsilane, pentamethyldisiloxane, phenyltetramethyldisiloxane and 1,1,1,3,5,5,5-heptamethyltrisiloxane to form 4-(phenyldimethylsilyl)-1-bromobutane (**14**), 4-bromobutylpentamethyldisiloxane (**16**), 1-(4-bromobutyl)-3-phenyltetramethyldisiloxane (**17**) and 3-(4-bromo)butylheptamethyltrisiloxane (**18**), respectively. It can also be hydrosilylated with chlorodimethylsilane, and immediately hydrolyses to form the known compound 1,3-bis(4-bromobutyl)tetramethyldisiloxane (**15**). **14** reacts with thymine, adenine and cytosine to form **12**, 4-(phenyldimethylsilyl)-9-butyladenine (**19**) and 4-(phenyldimethylsilyl)-1-butylcytosine (**20**), respectively. **20** has been structurally characterised.

Chapter 5 describes the reaction of thymine and adenine with compounds **15-18**, and the reaction of cytosine with **15**, in the presence of potassium carbonate. Thymine reacts with **15** to form 1,3-bis(1-butylthymine)tetramethyldisiloxane (**21**) and 6,6,8,8,15-Pentamethyl-7-oxa-1,13-diaza-6,8-disila-bicyclo[11.3.1]heptadec-15-ene-14,17-dione (**22**), with **16** to form

4-pentamethyldisiloxy-1-butylthymine (**23**) and with **18** to form 3-(1-butylthymine)heptamethyltrisiloxane (**24**). Adenine reacts with **15** to form 1,3-bis(1-butyladenine)tetramethyldisiloxane (**25**), with **16** to form 4-pentamethyldisiloxy-1-butyladenine (**26**) and with 18 to form 3-(1-butyladenine)heptamethyltrisiloxane (**27**). Cytosine reacts with 15 to form 1,3-bis(1-butylcytosine)tetramethyldisiloxane (**28**) and 16-Imino-6,6,8,8-tetramethyl-7-oxa-1,13-diaza-6,8-disila-bicyclo[11.3.1]heptadec-14-en-17-one (**29**). 22 and 29 have been structurally characterised.

Chapter 6 concerns the formation of thymine compounds with pendant imine-containing silyl groups *via* imine-formation reactions in the presence of magnesium sulphate. Allylamine can be hydrosilylated with phenyldimethylsilane to form (3-aminopropyl)phenyldimethylsilane (**30**). Thymine substitutes with α-bromo-*p*-tolualdehyde in the presence of potassium carbonate to form 4-(5-Methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-ylmethyl)benzaldehyde (**31**), which has been structurally characterised. Benzaldehyde reacts with **30** and (3-aminopropyl)diethoxymethylsilane to form [3-(Dimethyl-phenyl-silanyl)-propyl]-[1-phenyl-meth-(E)-ylidene]-amine (**32**) and [3-(Diethoxy-methyl-silanyl)-propyl]-[1-phenyl-meth-(E)-ylidene]-amine (**33**) respectively. **31** reacts with **30** and (3-aminopropyl)diethoxymethylsilane to form 1-(4-{[(E)-3-(Dimethyl-phenyl-silanyl)-propylimino]-methyl}-benzyl)-5-methyl-1H-pyrimidine-2,4-dione (**34**) and 1-(4-{[(E)-3-(Diethoxy-methyl-silanyl)-propylimino]-methyl}-benzyl)-5-methyl-1H-pyrimidine-2,4-dione (**35**). Paratolualdehyde reacts with 3-bis-(3-aminopropyl)tetramethyldisiloxane to form {3-[1,1,3,3-Tetramethyl-3-(3-{[1-p-tolyl-meth-(E)-ylidene]-amino}-propyl)-disiloxanyl]-propyl}-[1-p-tolyl-meth-(E)-ylidene]-amine (**36**). **31** reacts with a PDMS containing 2% aminopropyl functionality to form a PDMS containing 2% thymine functionality *via* an imine linkage.

Finally, chapter 7 concerns the formation of siloxane polymers containing pendant butyl DNA base functionality. **18** reacts with a PDMS of Mw approximately 50,000 to form a PDMS with approximately 0.2% bromobutyl functionality (**37**), and with a PDMS of Mw approximately 25,000 to form a PDMS with approximately 0.5% bromobutyl functionality (**38**). **37** and **38** react with thymine and adenine in the presence of potassium carbonate to form siloxane polymers with approximately 0.2% thymine (**39**), 0.5% thymine (**40**), 0.2% adenine (**41**) and 0.5% adenine (**42**) functionality.

Acknowledgements

First and foremost, I wish to thank Professor Kieran Molloy for his constant and involved interest in the work I have done. His wealth of experience and knowledge, in both the direction of practical work and its subsequent reporting, has guided me with care and attention from the morning I first stepped into the laboratory to the evening I handed in this thesis. Similarly, I would also like to thank Dr. Gareth Price for his involvement in the direction of my work, particularly in the areas of the polymer chemistry carried out in the final year of research, and Richard Taylor and Ian McKinnon at Dow Corning for their interest, not only as representatives of my corporate sponsor, but as chemists being shown new, and in some cases unexpected results.

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Finally, on a more personal note, there are more people that deserve my gratitude for one thing or another than there is space for me to offer it to them, so I will cite only the most important of cases. Firstly, I wish to thank my girlfriend Emma, who has put up with my working odd hours, stressing over results and, in the writing up stages, passing her like a ship in the night on regular occasions as I worked late into the night while she slept, without ever so much as a raised eyebrow. Secondly, and most importantly of all, I wish to thank Nick and Glynis, my parents. Their guidance, support and unquestioning love to me for the entirety of my life, something I may not have always been as receptive to as I should, has encouraged me to follow my heart and my dreams, rather than my pessimism. Look where it has got me.

Abbreviations

°	Degrees
Å	Angstroms
A	Adenine
atm	Atmospheres
C	Cytosine
C_{ad}	Carbon atom in adenine group
C_{benz}	Carbon atom in benzyl group
C_{cy}	Carbon atom in cytosine group
cm^3	Cubic Centimetres
C_{ph}	Carbon atom in phenyl group
Cs	Centistokes
C_{ty}	Carbon atom in thymine group
D	Doublet
DC	Direct Current
DCM	Dichloromethane
DMF	Dimethylformamide
DMSO	Dimethylsulphoxide
DNA	Deoxyribonucleic Acid
dppf	1,1'-Bis(diphenylphosphino)ferrocene
DSC	Differential Scanning Calorimetry
dt	Doublet of Triplets
DTBM	Di-tert-butyl maleate
Et	Ethyl Group
F	Degrees Farenheit
Fig	Figure
g	Grams
G	Guanine
GPC	Gel Permeation Chromatography
h	Hours
HMDS	Hexamethyldisilazane
HMTS	1,1,1,3,5,5,5-heptamethyltrisiloxane
HMTSBuBr	3-(4-bromo)butylheptamethyltrisiloxane
Hz	Hertz
IR	Infra-Red Spectroscopy
J	Coupling Constant
K	Degrees Kelvin

$kJmol^{-1}$	Kilojoules per mole
Lit	Literature Value
m	Multiplet
Me	Methyl Group
mg	Milligrams
MHz	Megahertz
mmol	Millimoles
Mn	Number average molecular weight
mp	Melting Point
Mw/Mn	Polydispersity
NaH	Sodium Hydride
NMR	Nuclear Magnetic Resonance
OAc	Acetyl Group
°C	Degrees Celsius
OMCTS	Octamethylcyclotetrasiloxane
$Pd(PPh_3)_4$	*tetrakis*-(triphenylphosphine) palladium
PDMS	Polydimethylsiloxane
Ph	Phenyl Group
PhDMS	Phenyldimethylsilane
PhTMDS	Phenyltetramethyldisiloxane
PMDS	Pemtamethyldisiloxane
ppm	Parts per million
r	Relative travel distance (TLC)
R	Alkyl Group
s	Singlet
SEGPHOS	4,4-bi-1,3-benzodioxole)-5,5-diylbis(diarylphosphine)
$SiMe_3$	Trimethylsilyl Group
t	Triplet
T	Thymine
TBAF	Tetrabutylammonium Flouride
^tBU	Tertiary Butyl Group
THF	Tetrahydrofuran
TMDS	Tetramethyldisiloxane
TMS	Trimethylsilyl Group
V	Viscosity
VI	Viscosity Index

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Chapter 1

Introduction

1.1 Preface

This thesis concerns the synthesis and characterisation of a siloxane polymer with pendant DNA bases at regular intervals. In order to introduce the work, chapter one will briefly review the structure and chemistry of DNA, the recent work in the area of substituted DNA bases, and address the methodology used in the proposed synthesis. It will go on to briefly review inorganic polymers containing silicon, and address the applications of similar organic polymers and contrast their potential with those of the target family of molecules in this investigation. It will conclude with an overview of the aims of the work and proposed methods of achieving them.

1.2 History of the chemistry of the DNA bases

1.2.1 Structure of DNA

Deoxyribonucleic acid (DNA) was discovered by Miescher in 1869 as a weakly acidic substance in human white blood cells. Lack of reliable analytical methods prevented further investigation until 1929, when Levine[1] reported the presence of four bases in the structure: the purines adenine and guanine, and the pyrimidines thymine and cytosine. In 1949, Chargaff[2] reported equal amounts of adenine and thymine, and cytosine and guanine **(Fig 1.3)** in the structure.

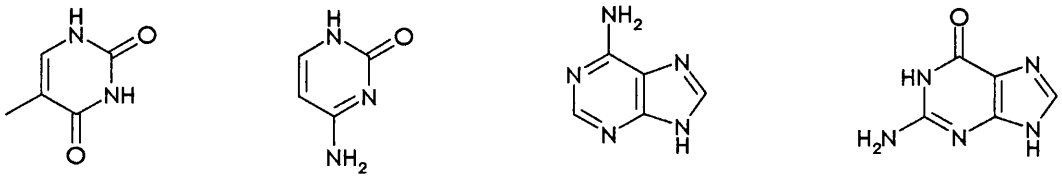


Fig 1.3. Left To Right: Thymine, Cytosine, Adenine and Guanine

In 1953, two different potential structures of the molecule were published by Pauling and Corey,[3] suggesting a triply helical structure, and Watson and Crick[4] (**Fig 1.4**[5]) who suggested a doubly helical structure they thought had greater stability. The latter model was subsequently accepted as correct and earned Watson, Crick and Wilkins the Nobel prize.

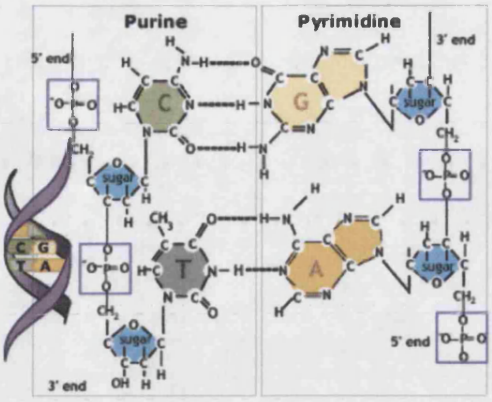


Fig.1.4. Watson-Crick DNA Structure

1.2.2 Hydrogen-bonding in DNA bases

The Watson-Crick pairing of DNA bases shown in **Fig 1.4** in which adenine shares two hydrogen bonds with thymine, and guanine shares three with cytosine, is one of several reported hydrogen bonding modes adopted by the bases. There are twenty-eight reported multiple hydrogen bonds motifs that can be formed between the four bases.[6] All of the bases are known to homodimerise, and pairs of bases can adopt non-Watson-Crick motifs limited only by the available sites for hydrogen bonding. Reverse Watson-Crick bindings involve the same hydrogen bonding sites but with one base inverted with respect to the Watson-Crick binding (**Fig. 1.5**).

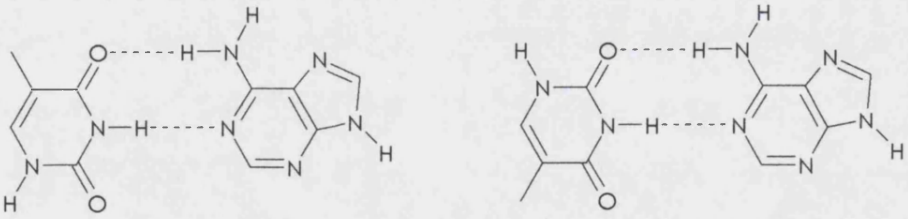


Fig. 1.5. Orientation Differences In Watson-Crick (Left) and Inverted Watson-Crick Base Pairing Between Adenine-Thymine

Hoogsteen parings[7] involve the pyrimidine binding to a different site, the Hoogsteen site, on the purine (**Fig. 1.6**).

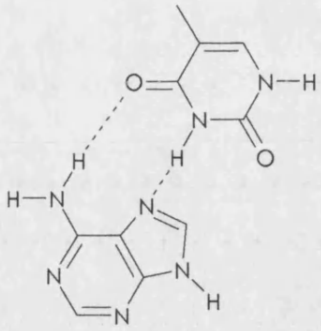


Fig. 1.6. Hoogsteen Base Pairing in Adenine-Thymine

Other pairings tend to be referred to as Wobble or Mismatched bindings.[8] Making use of both bonding sites on the purine, more complex motifs involving three bases, known as base-triplets, can form[9] and are found in examples of triple helix DNA.[10] In addition to homodimerisation, the purine bases can make use of their multiple hydrogen bonding sites to aggregate into polymeric tapes[11] and macrocycles capable of stabilising metal centres.[12] Monomeric DNA bases can also bind metal centres via hydrogen bonding, either alone or complexed with another group[13].

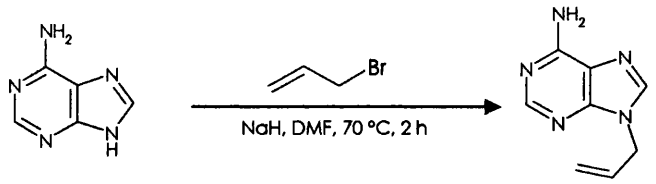
1.2.3 Substitution reactions to DNA bases

The functionality present in the four bases is extensive. Thymine, cytosine and guanine all contain carbonyl groups, and all the bases contain primary or secondary amines. The oxygen atoms in thymine are particularly susceptible to electrophilic attack as the residual electron density can be brought into the ring establishing aromaticity. This method can be used to add alternate functionaility to the bases, either directly or as a precursor to a polymer chain.

In order to form a siloxane polymer containing pendant DNA base functionality, some method of linking the polymer and base together needs to be achieved. Direct reaction of electrophiles at nucleophilic atoms such as oxygen and nitrogen are common in organic chemistry, and have been used as a method to add various functional and alkyl chains to the bases, discussed below. It was suggested that a suitable reaction sequence utilising a silicon species attached to an electrophilic alkyl group may form the basis for a polymer and associated model compounds of the desired type, so it is of interest to review the literature surrounding substitution of electrophiles at DNA bases.

Complications can arise in such reactions where there is more than one potential reaction site on the molecule, as is the case with the DNA bases. Directing the regiochemistry of the reaction then becomes important in order to prevent side reactions which will lower the yield of the desired products. Early attempts to alkylate protected bases involved the substitution of dibromoalkanes under very mild conditions to avoid the unwanted side-reactions. Brown showed that under these conditions, in reactions several days in length, alkyl groups could be added to protected thymine in reasonable yields, though were still susceptible to side reactions.[14] He also showed the addition of bromoalkanes to unprotected thymine was possible, but in lower yield and still taking considerable time.[14]

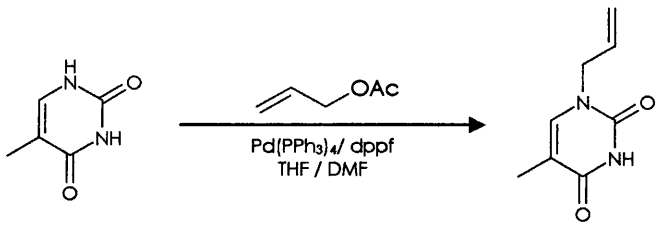
As a means to affect the regiochemistry of the reaction, the bases can be protected in order to limit the sites that reaction can take place. Deleris *et al*[15] found that silylating the molecule prior to the reaction offered better yields and a shorter reaction time than reported by Brown. However, they found that by making use of sodium hydride as a proton acceptor, direct addition of bromoolefins to the other three bases was possible, as in the addition of allyl bromide to adenine (1).



(1)

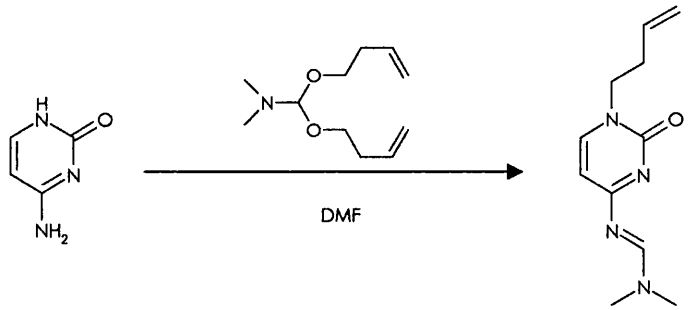
Larger substituents have been introduced onto the bases using Lewis acids as catalysts to improve yields and selectivity.[16, 17]

Alternative strategies for alkylation without protection are varied. Allyl acetate and a palladium catalyst was used by Amblard[18] as a method by which an allyl group could be added to unprotected thymine (2).



(2)

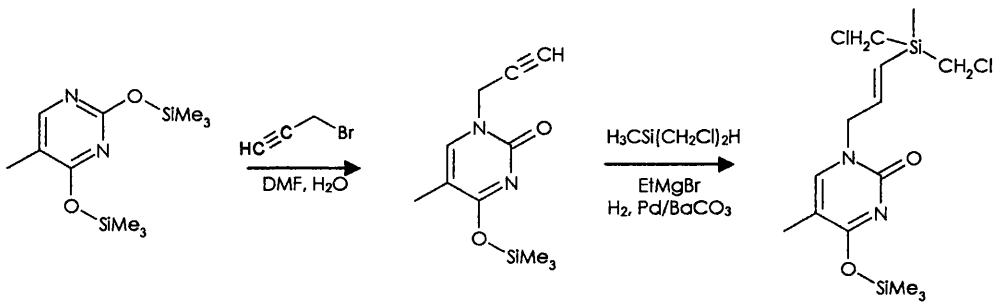
Also, strategies were presented that both protected and added the groups in one stage, such as the method reported by Furuta,[19] who used dimethylformamide dialkenylacetal to protect the free amine of cytosine and simultaneously add to its unhindered ring nitrogen (3).



(3)

Subsequent deprotection with sodium hydroxide yielded the free butenyl cytosine.

Recently, Thibon[20] *et al* reported the possible precursor to a siloxane polymer in a synthesis in several steps of a thymine molecule with a pendant silylalkene group containing chlorine atoms, bearing resemblances to the dimethyldichlorosilane precursor to PDMS (4).



(4)

It was suggested that hydrolysis of the chloride groups would lead to polymerisation and the formation of a siloxane polymer.

The addition of alkyl and alkenyl groups to DNA bases has been important due to the current interest in the production of synthetic nucleotides and nucleosides, described below. Most strategies involve the substitution reaction between a halide or acetate on the organic group, with either the free proton attached to a nitrogen atom on the base in the presence of a transition metal catalyst in the case of acetate, or with a protecting group such as TMS in the

case of the halide. Prior protection of the bases has generally allowed for more vigorous reaction conditions, allowing the reactions to take less time than the lengthy syntheses reported in the earlier literature.[15] All four bases have been protected with silyl groups, *via* various experimental methods.

The bases can be reacted with trimethylsilylchloride and triethylamine, and the product distilled out of the reaction mixture.[21] Kim[22] found greater yields and cleaner products obtained from the reaction of adenine and thymine with hexamethyldisilazane, using trimethylsilylchloride as a Lewis acid. Finally, Wittenburg[23] replaced trimethylsilylchloride with ammonium sulfate and achieved good yields and high purity of silylated pyrimidines.

1.3 Hydrosilylation

Hydrosilylation is the addition of silicon and hydrogen across a C=C double bond to form a saturated organosilane. This reaction plays significant roles in various areas of synthesis, particularly in the area of polymer chemistry where the reaction can be used to graft alkyl chains to silicon surfaces[24] and chains,[25] or to crosslink a structure and form three-dimensional networks. The first reported synthesis using this method was in 1947 by Sommer,[26] who was able to prepare n-octyltrichlorosilane from 1-octene and trichlorosilane, in the presence of catalytic diacetyl peroxide (5).

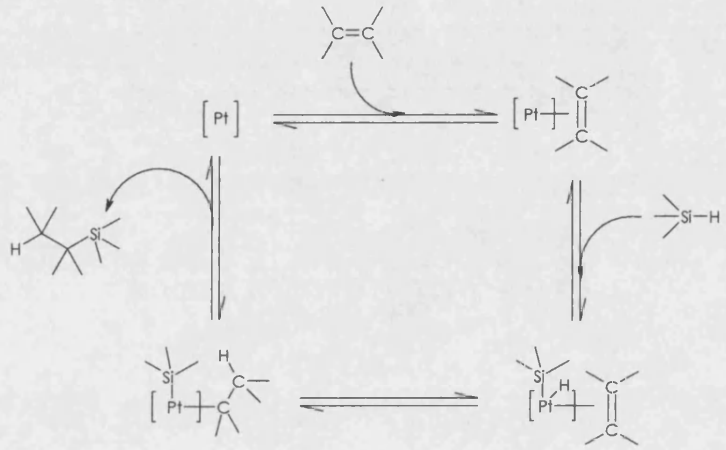
$$CH_3(CH_2)_5CH{=}CH_2 + HSiCl_3 \xrightarrow{(CH_3COO)_2} CH_3(CH_2)_5CH_2CH_2SiCl_3 \qquad (5)$$

He believed this to occur by a radical mechanism, where the peroxide split into two radicals, then again, forming a methyl radical and carbon dioxide. The methyl radical reacts with the trichlorosilane to form a silyl radical and methane. The silyl radical then adds to the olefin and reacts with another molecule of trichlorosilane to propagate the reaction.

In subsequent years, hydrosilylation research centred mainly on development of new catalysts to improve the process. Azo-compounds were reported to catalyse the reaction,[27] as was platinum,[28] and the heating of the reaction to high temperatures,[29] although the temperatures reported (in the region of 300°C) limited the number of useful reagents.

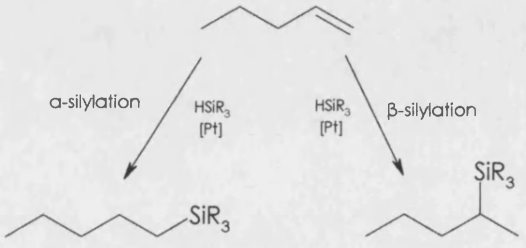
The major breakthrough in hydrosilylation chemistry was made by Speier and coworkers in 1956, with the reported the use of chloroplatinic acid, H_2PtCl_6, as a catalyst[30] in

the second paper in a series of twelve on hydrosilylation published between 1956 and 1970. In the first paper, he had elaborated on the use of peroxides as catalysts,[31] but showed in the second that chloroplatinic acid, and to a lesser extent, platinum black, was a superior catalyst and gave the best results over a number of different reactions. Hydrosilylation follows the mechanism proposed by Chalk and Harrod,[32] shown in **Scheme 1.1** below, the metal centre acting as both a co-ordination site for the olefin, and a site for Si-H bond cleavage.



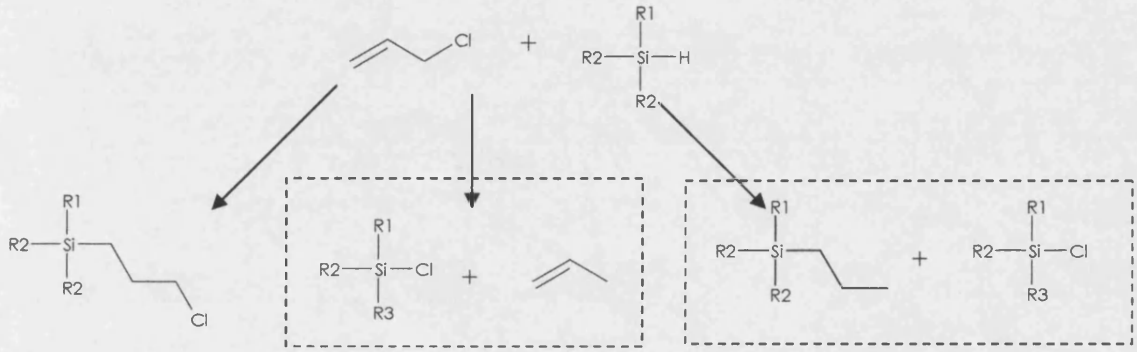
Scheme 1.1. Chalk-Harrod Hydrosilylation Mechanism

The mechanism first involves the π co-ordination of the olefin to the metal centre. The silane then oxidatively adds to the metal across the Si-H bond. The H migrates to the β-carbon on the olefin, prompting it to change from π- to σ-co-ordination to the metal. The complex then undergoes internal rearrangement, eliminating the alkylsilane and regenerating the metal centre for another cycle. Very recently, a new mechanism has been suggested for certain complexes including ruthenium catalysts,[33] bearing some similarity to the Chalk-Harrod system. It is also possible for the silyl and hydride groups to add in the other direction across the bond (the hydride to the α-carbon and the silyl group to the β-carbon). When the olefin contains more than two carbon atoms, this can produce unwanted side products (**Scheme 1.2**).



Scheme 1.2. Potential For Side Reactions In The Hydrosilylation Of Olefins

The twelve papers published by Speier were a detailed account of investigations into a wide range of different hydrosilylation reactions, and dealt with the addition of Si-H across terminal,[30] internal,[34] branched,[35] and halogenoolefins.[36, 37] Further investigation of the reactions with allyl groups and a variety of silanes followed, and varying results were obtained. Either the desired hydrosilylation product was obtained, or a substituted silane and propene were produced, or, finally, the nascent propene itself would undergo hydrosilylation in solution to produce an unfuctionalised alkylsilane, shown in **Scheme 1.3.**



Scheme 1.3. Other Potential Side Reactions In The Hydrosilylation Of Olefins

Both pressure and nature of catalyst are factors in the outcome of the reactions. Higher pressures produced more of the unwanted by-products, whereas atmospheric pressure reactions produced higher yields of the desired hydrosilylation product. The use of palladium on carbon, rather than chloroplatinic acid, resulted almost entirely in the production of propene. Further investigations were carried out involving varying the silicon hydride, and the reactions with siloxanes,[38, 39] aminosilicon hydrides and silazanes.[40]

Other hydrosilylation catalysts have been reported to have activities comparable to that of Speier's catalyst. Rhodium(II) and (III) complexes, such as *tetrakis*(μ-acetato)dirhodium(II), *tris*(pentanedionato)rhodium(III) have shown significant hydrosilylation activity.[41] Copper(I)[(-)DTBM-SEGPHOS][42] and ((R)-(+)-4-isopropyl-2-(2-pyridinyl)-2-oxazoline)Pd(Me)Cl have been shown to catalyse asymmetric hydrosilylations in good yield and high enantiomeric excess.[43] Iridium-based catalysts such as [*tris*(diphenyloxophosphoranylmethanide)]iridium-*bis*(ethene) have been shown to be active in the hydrosilylation of ethene,[44] whereas osmium compounds such as $OsHCl(CO)(P^iPr_3)$ have been found to be catalytic to the hydrosilylation of alkynes.[45] Research has also

encompassed the wide-ranging uses of hydrosilylation in synthesis, and new uses for this reaction are constantly being reported, as a reaction step that gives reasonable yields under relatively mild conditions.

1.4 Silicon-containing polymers

1.4.1 Polysiloxanes

Polysiloxanes, or silicones, were first reported in a series of papers by Kipping,[46] as part of the results of a thirty-year study of the silyl analogues of common organic compounds. The Si-OH group, readily available *via* hydrolysis of a silyl chloride, is susceptible to condensation, eliminating water to form the silyl equivalent of an ether (6).

$$2R_3SiCl \xrightarrow{2H_2O} 2R_3SiOH \xrightarrow{Fast} R_3SiOSiR_3 + H_2O \qquad (6)$$

Kipping named the new Si-OH compounds *silicols*, and found them much more susceptible to condensation elimination to form *silico-ethers* than their organic equivalent, which require acid catalysis and a dehydrating agent. It was observed that the diorganosilyl dichlorides are even more susceptible to hydrolysis (7), and subsequently condense so readily that *silicodiols* are hard to crystallise, though examples do exist where R is large e.g. ^tBu[47] or ferrocene.[48]

$$R_2SiCl_2 \xrightarrow{2H_2O} R_2Si(OH)_2 + 2HCl \qquad (7)$$

Rather than isolating a condensation product analogous to a ketone, the reluctance of silicon to form double bonds lead it to form linear and cyclic oligomeric structures as its condensation product (8). Despite this difference to their organic equivalent, Kipping continued to draw parallels with his terminology and named them *silicones*.

$$4R_2Si(OH)_2 \longrightarrow HO\text{—}\underset{\displaystyle R}{\overset{\displaystyle R}{\underset{\displaystyle R}{\overset{\displaystyle R}{Si}}}}\text{—}O\text{—}\underset{\displaystyle R}{\overset{\displaystyle R}{\underset{\displaystyle R}{\overset{\displaystyle R}{Si}}}}\text{—}O\text{—}\underset{\displaystyle R}{\overset{\displaystyle R}{\underset{\displaystyle R}{\overset{\displaystyle R}{Si}}}}\text{—}O\text{—}\underset{\displaystyle R}{\overset{\displaystyle R}{\underset{\displaystyle R}{\overset{\displaystyle R}{Si}}}}\text{—}OH + 4H_2O \qquad (8)$$

It is possible to isolate some of the cyclic oligomers as crystals where R is large e.g. Ph. However, where R is small e.g. Et, the products are higher polymers of varying molecular

weight in an amorphous mass. Kipping referred to them as "glue-like", and did not consider them chemically valuable.

Contemporary to Kipping's investigation, work was being carried out by Alfred Stock[49] on derivatives of silane, SiH_4, in the gas phase. Dichlorosilane can be prepared from silane using hydrogen chloride and a Lewis acid (9).

$$SiH_4 + 2HCl \xrightarrow{AlCl_3} 2H_2 + SiH_2Cl_2 \qquad (9)$$

In turn, this reacts with dimethyl zinc to form a dimethylsilane, still a gaseous product (10).

$$SiH_2Cl_2 + (CH_3)_2Zn \longrightarrow (CH_3)_2SiH_2 + ZnCl_2 \qquad (10)$$

When this is allowed to condense on frozen alkaline solution and then warm slowly, it undergoes hydrolysis to form dimethyldihydroxysilane, which immediately condenses in the same way as Kipping's products to form a polymeric structure (11).

$$(CH_3)_2SiH_2 + \xrightarrow{2H_2O} (CH_3)Si(OH)_2 \longrightarrow [(CH_3)_2SiO]_n + H_2O \qquad (11)$$

The gas phase nature of the reactions placed severe limitations on the amounts of reagents that could be used, and as a result the product was never isolated. Kipping would have referred to it as *methyl silicone*, while Stock used a different system to name it *polydimethylsiloxane* (PDMS), and his nomenclature survives to the present day.

In 1940, the synthesis of PDMS without the use of organometallic reagents was achieved by Eugene Rochow[50], by reacting hydrogen chloride with a Cu-Si alloy (as a source of both silicon and catalyst in one substance), which etches the surface of the alloy forming trichlorosilane and exposing a fresh silicon surface (12).

$$nSi + 3HCl \longrightarrow SiHCl_3 + H_2 + (n-1)Si \qquad (12)$$

Chloromethane then reacts with the fresh surface and undergoes various reactions, resulting in dimethyldichlorosilane (13).

$$2CH_3Cl + Si \longrightarrow (CH_3)_2SiCl_2 \qquad (13)$$

Finally, the hydrolysis of the product produces the corresponding diol (14), which immediately undergoes partial condensation to form siloxanes. Upon heating, these siloxanes condense further to produce PDMS (15). This method has become the general procedure for the synthesis of PDMS, and bears Rochow's name.

$$(CH_3)_2SiCl_2 \xrightarrow{2H_2O} (CH_3)_2Si(OH)_2 + 2HCl \qquad (14)$$

$$2(CH)_3Si(OH)_2 \xrightarrow{-H_2O} HO-\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{Si}}-O-\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{Si}}-OH \xrightarrow{-H_2O} [(CH_3)_2SiO]_n \qquad (15)$$

1.4.1.1 Chemistry Of Polysiloxanes

Siloxane polymers are physically more flexible than their carbon counterparts, due to the nature of the siloxane backbone. The Si-O-Si bond angle is of the order of 143°, and can vary between 109° and 180°,[51] a considerably wider range than that of a C-C bond. This serves to increase the dynamic flexibility of the chain,[52] which refers to the molecule's freedom to change conformation about its skeletal bonds. High dynamic flexibility leads to a low glass transition temperature. As shown below (**Fig.1.1**), the Si-O bond length is 1.64Å, considerably longer than the C-C bond length of 1.53Å, lowering steric congestion within the molecule.[52] This has an effect on equilibrium flexibility, which refers to the chain's radius of gyration in the absence of excluded-volume effects.[53]

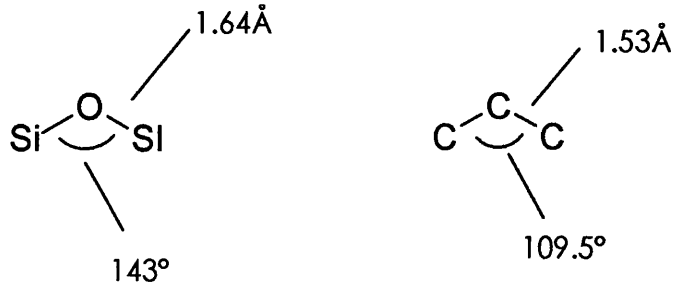


Fig 1.1. C-C / Si-O-Si Chain Comparison

Also, the oxygen atoms in the backbone are unhindered by side chain groups, and are the smallest centres about which two chain bonds can form. PDMS, with its small side groups and siloxane backbone, has the lowest glass transition temperature of any known polymer, becoming brittle at ~-125 °C.[54]

The commercial significance of siloxane polymers lies almost entirely in the varying chemistry of PDMS, and how it can be tailored to produce polymers with different structural characteristics through the application of cross-linking and chain termination steps. PDMS itself has several physical characteristics that have made it a commonly used substance in many applications. It has a very high electrical resistance ($4x10^{13}$ Ωm^{-1} [55]), so is used as an electrical insulator. It is highly unreactive, almost inert, and so can be used in medical applications without being toxic. Its also has a very high temperature resistance relative to its equivalent hydrocarbon polymers due to its inertness, enabling its use in high temperature systems where other polymers would fail.

1.4.1.2 Silicone Resins

A silicone resin is a solid siloxane polymer with a highly cross-linked structure. In the case of PDMS resin, this is formed by the mixing of dimethyldichlorosilane and methyltrichlorosilane before hydrolysis, subsequently forming the respective diols and triols which condense to form siloxane chains with extra Si-OH side groups. These groups subsequently condense further, forming a Si-O-Si link between two polymer chains. Heating drives this forward until any remaining Si-OH groups are too tightly bound in the structure to condense with others and so the process stops. The resulting material is insoluble and infusible, and it said to have been *cured* (**Fig 1.2**).

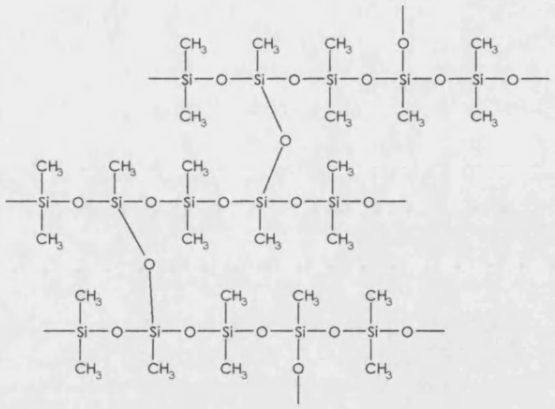


Fig 1.2 PDMS Silicone Resin Structure

Other methods for crosslinking involve the mixing of some trichlorosilane or methyldichlorosilane with the starting silane, producing Si-H groups in the resulting polymer chains that are very susceptible to oxidation into Si-O-Si cross-links.[56]

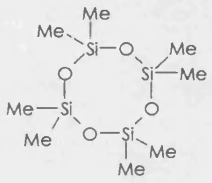
The cured material has excellent resistance to heat and oxidation, and coupled with the high electrical resistance of PDMS makes it an ideal insulator for high voltage machinery. Previous insulators had been much less resistant to heat and oxidation, and machines had had to be made very large, so as to dissipate the heat they produced more effectively whilst remaining within the limits of the insulator's working temperature. The introduction of silicone resins with their higher operating temperature allow machines to run hotter, enabling them to be built smaller and more compact.

A problem with using PDMS resins as protective coatings is their having to be in position on the surface they are protecting before they are cured, for there is no way of transferring them once the curing has taken place. To achieve this, the partially condensed resin is dissolved in a volatile solvent (silanols, like alcohols, are readily soluble in water-tolerant solvents such as ethanol and diethyl ether), and applied to the surface. As the solvent evaporates, the silanols condense and cure *in situ*. To prevent the cracking and splitting of the resin as it condensed, iron trichloride improves the integrity of the drying polymer and allows it to dry into a suitable layer without splitting apart.[57] This method of *in situ* curing opens up a wider range of uses for silicone resins. Glass fibers can be introduced to the resin, solidifying as it dries and forming fibreglass. This material finds widespread use as a building material and is still one of the most effective electrical insulators currently available. If a thermally stable pigment is added to the resin, the result is a heat resistant paint that can be used to protect hot metal surfaces that would cause normal paints to blister and crack. They are also

highly water resistant and can be applied to buildings and boats to protect them from weather and during constant immersion in water.

1.4.1.3 Silicone Oils

Where a resin is a solid macromolecule with a highly cross-linked structure, other forms of polymer are accessible. The prospect of utilising the thermal stability of PDMS in a lubricating agent is intriguing, but requires the ability to limit the chain lengths in order to produce an oil with relatively low viscosity. A method for doing this was found by Patnode.[58] Octamethylcyclotetrasiloxane ($(Me_2SiO)_4$) is the most stable cyclic oligomer of dimethylsiloxane, obtained first by Kipping[46]. While a stable molecule, the ring has exposed silicon atoms and is susceptible to opening. When added to concentrated sulphuric acid, the nature of the ring allows the acid to attack the Si-O linkages (normally completely inert to sulphuric acid), and form acid-soluble sulphate esters analogous to dimethyldichlorosilane (16).



$$+ \quad 8H_2SO_4 \longrightarrow 4(CH_3)_2Si(HSO_4)_2 + 4H_2O \qquad (16)$$

When added to excess water, this ester rehydrolyses, forming different products (17). The resulting siloxane is now formed of linear oligomers of varying lengths, with fundamentally different properties to the starting material.

$$(CH_3)_2Si(HSO_4)_2 + H_2O \longrightarrow ((CH_3)_2Si)_n(OH)_2 + 2H_2SO_4 \qquad (17)$$

On its own, this is not very useful, as with continuing heat, the polymer continues to condense until the chains become long enough for the polymer to become solid. However, Patnode had the idea to introduce chain terminating groups in the form of trimethylsilyl (TMS) fragments. Utilising the same method as above with hexamethyldisiloxane as a source of TMS groups, it is possible to produce their acid-soluble sulphate esters (18).

$$(CH_3)_3SiOSi(CH_3)_3 + H_2SO_4 \longrightarrow 2(CH_3)_3Si(HSO_4) + H_2O \quad (18)$$

Therefore, the mixing together of OMCTS and hexamethyldisiloxane in a 1:1 ratio, and the addition of a catalytic amount of concentrated sulphuric acid produces a mixture of the sulphate esters with water as the by-product. This water is sufficient to hydrolyse the esters, liberating chain forming -$(CH_3)_2SiO$-units and chain terminating $(CH_3)_3SiO$-units in a 4:2 ratio. These combine, esterify, hydrolyse and recombine in a random fashion, giving a mixture of oligomers terminated by TMS groups. Statistically, the ratio of chain forming to chain terminating groups dictates the average size of the oligomers to be $(CH_3)_3Si$-O-[-$(CH_3)_2Si$-O-]$_4$-$Si(CH_3)_3$, referred to as D_4 units.

The lower oligomers are volatile and can be distilled out of the mixture, leaving a clear, colourless liquid that is soluble in organic solvents, and insoluble in water and other lubricating oils. A fundamental difference between the linear and cyclic oligomers (and more importantly the equivalent linear hydrocarbon oils) is the relative independence of viscosity with respect to temperature. **Table 1.1** shows the changes in viscosity with temperature of silicone lubricating oil and an equivalent hydrocarbon lubricating oil (100 VI Petroleum).

Table 1.1: Viscosity As A Function of Temperature Between Silicone Oil and Hydrocarbon oil

Temp (F)	V (Silicone) (Cs)	V (Hydrocarbon) (Cs)
210	40	10.8
100	100	100
0	350	11000
-35	660	230000
-70	1560	-

Silicone oils have found use as hydraulic fluids at temperatures which would render hydrocarbon oils useless e.g. in aircraft at high altitude. Silicone oils also share the high electrical resistance of PDMS, although to a much greater extent (DC Volume resistivity $7.9x10^4$ Ωm^{-1} [57]), and are also resistant to heat, so are used as dielectric fluids for insulation of high-powered electronic machinery. Furthermore, silicone oils have the same high resistance to chemical reaction as PDMS, especially with other organics, and being liquid can take any

shape required. This has allowed them to be used as internal cosmetic implants in the human body, for example in the rehabilitation of victims of breast cancer.

1.4.1.4 Silicone Elastomers

The other interesting possibility of PDMS chemistry is the utilisation of its thermal and chemical stability in a rubber form, as an alternative to organic rubbers. In order to achieve this, a linear polymer with an extremely high molecular weight and chains largely independent of each other, with only very little cross-linking to provide structure, is required. Hyde[59] found when dimethyldichlorosilane is hydrolysed, large amounts of $[Me_2SiO]_4$ are formed, and can be distilled out of the mixture. The remaining linear polymer and larger cyclics can be catalytically converted into more $[Me_2SiO]_4$, which again can be distilled away from the reaction. The result is a high yield of very pure $[Me_2SiO]_4$ that can be used to produce the polymer by ring-opening polymerisation, in the first stage of the rubber production. Hyde proceeded to polymerise the material under relatively mild conditions using catalytic solid potassium hydroxide, which slowly attacked the strained Si-O-Si linkages, opening the rings and forming potassium silanolates and water. These quickly hydrolysed to produce polymer, regenerating the potassium hydroxide and repeating the process. The high purity of the starting material ensured that no cross-linking or chain terminating groups were present in the reaction, so the chains increased in length until all of the $[Me_2SiO]_4$ was used up. The resulting product was an extremely viscous PDMS gum with a molecular weight in the order of 2,000,000 to 5,000,000 Daltons.

To produce a usable rubber from the gum necessitated it first being strengthened, and then cross-linked to give it some structure. Silicon dioxide particles, in the form of macromolecular SiO_4 tetrahedra, were found to be an excellent strengthening agent. The particles were able to "fit" alongside the polymer chains and greatly increase the overall strength of the gum.[57]

Cross-linking of the strengthened gum was found to be possible in two ways: Firstly, the gum can be heated with an internal or external crosslinking agent. This can be benzoyl peroxide, which oxidises some of the methyl groups and creates $SiCH_2CH_2Si$ cross-links.[60] It can also be achieved by the incorporation of some Si-H and $Si\text{-}CH{=}CH_2$ groups into the original polymer structure, which will catalytically hydrosilylate to create $SiCH_2CH_2Si$ links. Secondly, the gum can be cured at room temperature by the use of chemical agents, allowing it to be put in place as a liquid and cured over time, rather like the process of hardening silicone resins. This can be accomplished by combining two materials *in situ* – one a PDMS gum containing Si-H and $Si\text{-}CH{=}CH_2$ groups, the other, a paste containing catalyst that will

allow the two groups to hydrosilylate. The reaction proceeds at room temperature and the liquid slowly cures. Another method of doing this is to treat a slightly trifunctionalised PDMS gum with acetic anhydride, forming acetoxy groups from the free Si-OH. When this is exposed to air, the acetoxy groups slowly hydrolyse to form Si-O-Si cross-links and volatile acetic acid, which evaporates with a distinctive odour.

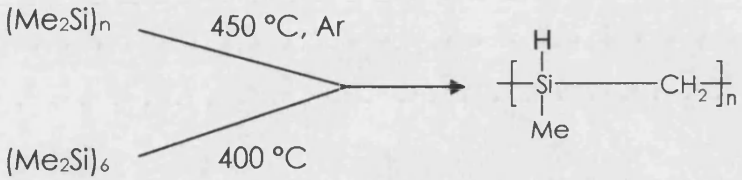
Like the other PDMS variants, these rubbers are highly thermally and chemically stable, and have high electrical resistance. Rubbers cured by the first method can be moulded into shape before curing, to produce whatever three-dimensional shapes are required. This, combined with their chemical inertness, has led to their being used in a very wide range of medical and cosmetic applications, both internally as catheter tubes etc., and externally as prosthetics of all types. The author has personal experience of the latter of these, in his hobby as a live-action roleplayer. This involves dressing up as a high fantasy character, camping in a field for several days and interacting with other like-minded people. In this alternative world he is an elf, so suitable prosthetic attachments to his ears, made from silicone rubber, are required to achieve a realistic looking character.

Rubbers of the second type, which cure where they are laid down, perform excellently as sealants and fixatives as they can be spread, piped or otherwise pressed into place, bind well to many different surfaces, and are resistant to weather and pollution.

1.4.2 Other Silicon-Containing Polymers

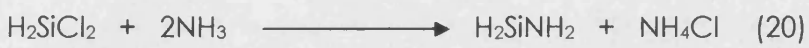
Various other polymers incorporating silicon in their structure have scientific or industrial significance. Polysilanes are polymers with backbones formed purely of silicon atoms, with two pendant groups on each silicon. In 1949, polydimethylsilane, $(Me_2Si)_n$, was synthesised by Burkhard[61] as an insoluble, infusible white powder, leading chemists to dismiss the entire family of materials as intractable. Later, West and co-workers[62] reported somewhat soluble silane copolymers of the type $Me_2Si/PhMeSi$ that appeared to melt when heated, leading to further work and the discovery of industrially significant properties of these materials. The silicon backbone of the polymer was observed to have a delocalised cloud of σ-electrons along its length, suggesting novel electronic and photochemical properties. Under UV light, polysilanes undergo photoscission to form silene radicals[63] which can cross link the polymer or catalyse other reactions such as a the polymerisation of olefins[64]. They can also be used as photoresists in either positive (polymer cross links after photoscission),[65] or negative (polymer decomposes on photoscission)[66] modes.

It is also possible, via heating in air or argon, to insert methylene groups into the backbone to form polycarbosilanes,[67, 68] (19).



(19)

The polycarbosilane can in turn be pyrolysed to form silicon carbide, one of the hardest known materials and a widely utilised industrial abrasive. The ammonolysis of the pyridine adduct of dichlorosilane, followed by subsequent polymerisation, forms polysilazanes,[69] (20, 21).



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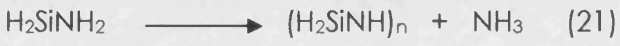
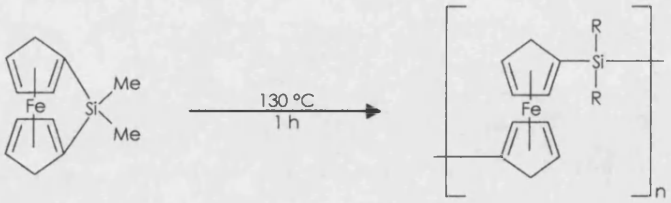


(21)

This can pyrolysed under varying conditions to form silicon nitride[70, 71] or silicon oxynitride,[72] both of interest in the ceramics industry. The reaction of dimethyldichlorosilane with a complexed dilithioferrocene and subsequent ring opening polymerisation leads to polyferrocenylsilane (22).



(22)

Pyrolysis of this material yields a magnetic ceramic containing Fe nanoparticles.[73] The nature of the magnetism can be tuned by altering the temperature of the pyrolysis, a property that may have applications in the fields of magnetic shielding and refrigeration.

1.5 Formation of Biomimetic Polymers

Recently, there has been interest in the functionalisation of polymer chains with biomimetic substituents, in attempts to produce synthetic polymers with the same properties as their naturally occurring counterparts.[74-76] Polymers analogous to nucleic acids have been made with easily synthesised vinyl, polypeptide or methacrylate polymers or oligomers with biologically functional pendant groups. Such polymers have potential biomedical applications.

In the same way that enzymes display very high selectivity in their catalytic activity, nucleic acids also display high selectivity due to the very structured positions of the bases on the backbone. Polymers have been synthesised containing nucleic acid functionality in an attempt to replicate the activity of the natural product. Poly(1-vinyluracil), synthesised by Pitha,[77] will form a conjugate with a polymer of its complimentary base, and together is active against certain forms of leukaemia.[78]

These types of polymer are also potentially useful in cancer therapy. Chemotherapy for cancer is difficult, due to the high toxicity of the drug agents relative to their anti-cancer activity. Single-chain polymers containing pendant nucleic bases could be used either directly as a enzyme-like catalyst for the production of antibodies, or indirectly as a method of delivery for nucleic base derivatives which can act as anti-cancer drugs.[79]

1.6 Project Aims

In the light of the potential use of siloxane polymers containing nucleic base functionality, and the novel chemistry they could display, it is therefore of interest to attempt a synthesis of monosiloxanes with pendant DNA bases, as a route to ordered hydrogen-bonded polymers. The proposed method to be followed in this work is displayed below **(Fig. 1.7)**.

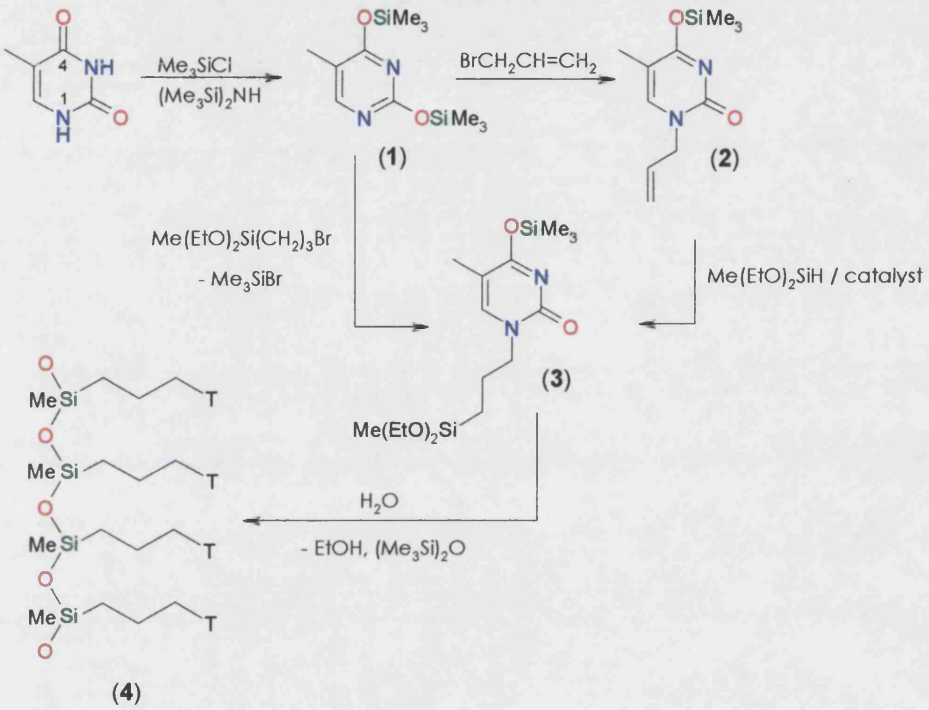


Fig 1.7. Intended Reaction Scheme

In both cases, the base is first protected with a silyl group **(1)**. Then, either a) the protected base is reacted with an alkenyl bromide, forming **(2)**, which can then be hydrosilylated with a silane, or b) the alkenyl bromide is first hydrosilylated by a silane and then reacted with the protected base, both methods leading to **(3)**. The final step involves the hydrolysis polymerisation to form the siloxane chain **(4)**. This thesis describes investigations of the different stages of the proposed reaction sequence, and their refinement and adaptation into a viable strategy for the production of this new class of polymers.

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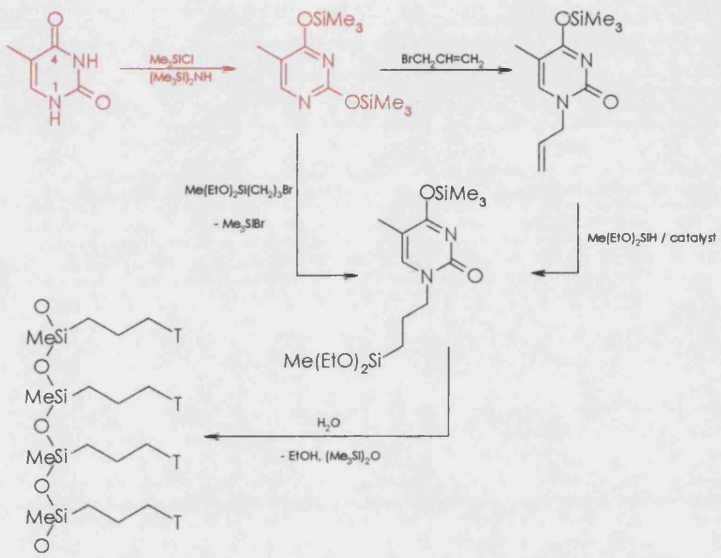
Chapter 2

Structural Characterisation of Trimethylsilyl-substituted DNA Bases

2.1 Introduction

The first step in the potential synthesis of a DNA base-containing polymer is the suitable protection of the bases (**Scheme 2.1**). This would prevent unwanted side reactions during the hydrosilylation step by sterically hindering the ring and ensuring only one uncrowded olefin at which to carry out the reaction.



Scheme 2.1

The protecting group would have to be easily removable under relatively mild conditions to prevent decomposition of product during recovery, and preferably generate by-products upon both protection and deprotection that are significantly physically different to the alkyl and alkenyl bases they would be separated from later in the synthesis. The silylated analogues of the bases are known,[1] and fitted the necessary criteria as the protecting groups are easily removable by hydrolysis and form liquid by-products. However, these silylated bases have never been structurally characterised, so it was of interest to synthesise crystalline samples for X-ray diffraction, in order to further investigate the hydrogen bonding modes of substituted DNA bases.

This chapter describes the structural characterisation of the four silylated bases and their hydrogen bonding patterns.

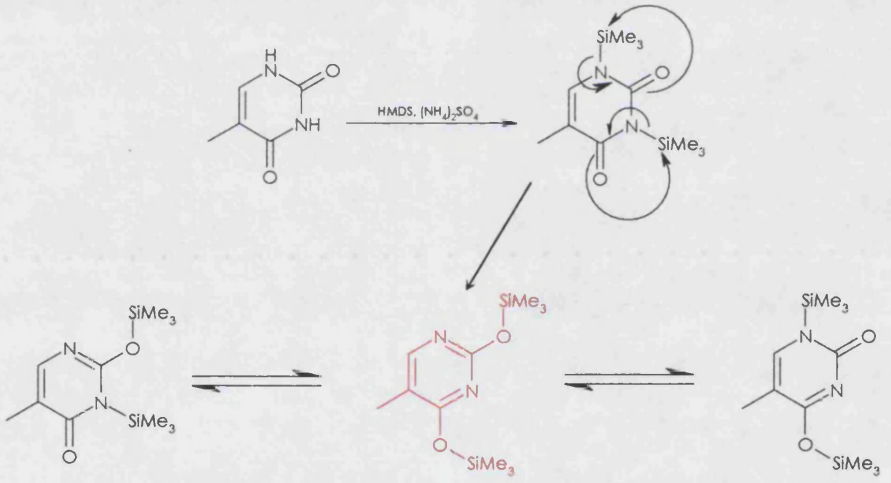
2.2 Synthesis of silylated DNA bases

A mixture of hexamethyldisilazane (HMDS), the DNA base in question and a few crystals of ammonium sulphate were refluxed until the opacity of the mixture due to solid base had cleared.[2] After removal of the volatiles, thick liquids remained that in three cases were purified by vacuum distillation to obtain the protected base, the product derived from thymine no requiring purification. Pertinent reaction and physical data are presented in **Table 2.1**. A representative reaction scheme and associated tautomerism is presented in **Scheme 2.1**.

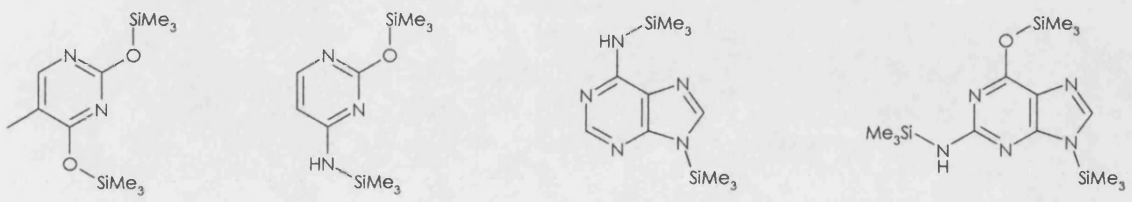
Table 2.1: Reaction Data For Protection of DNA Bases

	Reaction Time (h)	Yield (%)	Melting Point (°C)	Distillation Temp (°C/0.1atm)
1	20	93	128-30	Not distilled
2	20	20	128	200
3	72	50	130	240
4	144	72	121-3	250

Reported melting points for silylated bases: **1** 135-6°C,[2] **2** 122-3°C,[1] **3** 84-87°C,[1]



Scheme. 2.1. The silylation of thymine and tautomerism in the product



1 **2** **3** **4**

The melting points of **1** and **2** compared well with literature values, but that of **3** was significantly higher than reported previously (**Table 2.1**). It is possible that traces of HMDS remained in the sample of **3** previously tested, lowering its perceived melting point considerably from the true value. During the vacuum distillation of **3** and **4**, HMDS was observed to distil from the reaction mixture before the pure product was recovered. This HMDS had remained with the product during the removal of volatiles and could possibly have accounted for a lower recorded melting point than that observed in this investigation.

The driving force for the protection of the bases is different in each case. In the formation of **1**, the formation of two strong Si-O bonds, the aromatisation of the six-membered ring and associated resonance stability push the reaction forward strongly, making it the fastest of the protection reactions. It was also the only protection reaction generating a crude reaction mixture that showed peaks in the NMR corresponding to only the product. Similarly, by investigation of the ^{29}Si NMR data, the *bis* O-silylated tautomer was found to be the most stable, as two signals typically corresponding to silicon bonded to oxygen,[3] and none typically corresponding to silicon bonded to nitrogen,[4, 5] were observed (**Table 2.2**).

In the formation of **2**, the driving force is the formation of one strong Si-O bond, the aromatisation of the six-membered ring and the associated gain in resonance stability, but the formation of a slightly less strong Si-N bond (Si-O 466 kJmol^{-1},[6] Si-N 439 kJmol^{-1} [7]) involving the second protecting group makes the protection slightly slower than the formation of **1**. **2** also forms tautomers, the most stable highlighted in **Fig 2.1** by investigation of the ^{1}H and ^{29}Si NMR spectra. The ^{1}H spectrum showed a peak corresponding to one proton at δ = 4.19 ppm, suggesting that the primary amine was protected, and the ^{29}Si spectrum showed a peak typically corresponding to silicon bonding to oxygen,[3] suggesting that the ketone was protected, as well as a second peak corresponding to silicon in a chemically different environment.

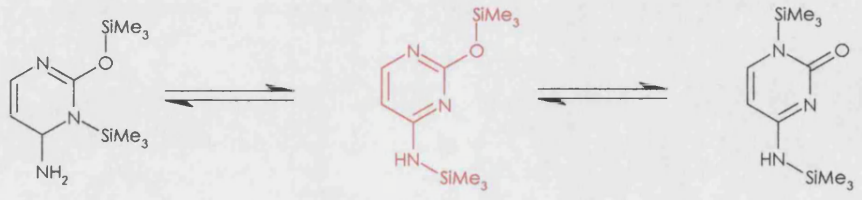


Fig. 2.1. $NSiMe_3$ / $OSiMe_3$ Tautomerism in 2

In the formation of **3**, the reaction is driven forward only by the formation of Si-N bonds. The purine rings are already aromatic, so there is no additional resonance stability associated with the protected base. The protection therefore takes significantly longer than in the cases of the pyrimidine protection reactions forming **1** and **2**.

The formation of **4** takes the longest of all of the reactions protecting the DNA bases with $SiMe_3$ groups. While it involves the formation of a strong Si-O bond and a subsequent aromatisation of the six-membered ring leading to resonance stabilisation, there are three sites to protect. Once the most favourable of these (the ketone group) has been protected, the other two have only the formation of Si-N bonds to drive them forward. As in the formation of **3**, this is not as favourable as the formation of Si-O, and no resonance stability is gained by doing so, so the protection proceeds slowly. The relative stability of the tautomers formed by **4** (**Fig. 2.2**) was assigned by investigation of the ^{29}Si NMR spectrum, which showed peaks corresponding to silicon bonded to oxygen, primary amine and secondary amine nitrogen atoms.

Fig. 2.2. NSiMe3 / OSiMe3 Tautomerism in 4

The ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of the four compounds were unremarkable, showing singlets due to TMS near to $\delta = 0$ ppm and resonances due to the base in good correlation with the literature.[5] Of greater interest, however, were the ^{29}Si NMR spectra of the compounds (**Table 2.2**), which illustrates well the different environments in which silicon was found in the protected compounds

Table 2.2: ^{29}Si NMR Data For Protected DNA Bases

	Solvent	^{29}Si NMR (δ)
1	Chloroform	20.8 (Si-O) 22.8 (Si-O)
2	Chloroform	7.2 (Si-NH) 20.9 (Si-O)
3	DMSO	7.2 (Si-NH) 14.3 (Si-N)
4	Benzene	3.4 (Si-NH) 13.4 (Si-N) 23.6 (Si-O)

These also correlate well with literature values,[5] and are assigned on the basis of known silicon shifts in other compounds (Me_3Si-OPh 19.23,[3] Me_3Si-NHSiMe_3 2.1,[4] Me_3Si-$N_{pyrrole}$ 12.04[5]).

2.3 Structure of bis-(trimethylsilyl)thymine (1)

Thin, needle-like crystals of **1** were formed spontaneously from a molten sample as it cooled. The molecular structure of **1** is illustrated in **Fig. 2.3**. Selected bond lengths and angles are presented in **Tables 2.3** and **2.4**. Crystal structure data are presented in **Appendix 8.2**.

The structure of the molecule is monomeric, with no intermolecular interactions. The two $SiMe_3$ groups have protected the ketone groups, the silicon atoms lying in the plane of the molecule, with relatively long bond distances [Si(1)-O(1) 1.6906(16) Å, Si(2)-O(2) 1.6951(16) Å] compared with silyl ether bonds in similar compounds[8-10] such as in *hexa*-(trimethylsiloxy)benzene [Si-O 1.655(3) Å, 1.673(4) Å].[10] There is a distortion of bond lengths in the ring as a result of the aromatisation caused by the protection [C(1)-N(2) 1.338(3) Å, C(5)-N(2) 1.327(3) Å, C(3)-C(5) 1.406(3) Å] relative to thymine [C(1)-N(2) 1.361(4) Å, C(5)-N(2) 1.401(5) Å, C(3)-C(5) 1.453(4) Å].[11]

The bulk of the $SiMe_3$ groups has caused the ring to distort slightly to accommodate them, opening the N-C-N bond angle in particular [N(1)-C(1)-N(2) 127.29(19)°], and closing the C-N-C bond angles [C(1)-N(1)-C(2) 114.85(19)°, C(1)-N(2)-C(5) 115.63(18)°] compared to the same angles in thymine [N(1)-C(1)-N(2) 115.5(2)°, C(1)-N(1)-C(2) 122.5(3)°, C(1)-N(2)-C(5) 126.3(3)°].[11] The bulk of the $SiMe_3$ group has forced it away from the ring, enlarging the C-O-Si bond angle [C(1)-O(1)-Si(1) 125.40(14)°, C(5)-O(2)-Si(2) 125.46(14)°] from the expected tetrahedral value.

Table 2.3: Selected bond lengths (Å) for bis-(trimethylsilyl)thymine (1)

C(1)-O(1)	1.341(3)	C(1)-N(2)	1.338(3)
O(1)-Si(1)	1.6906(16)	C(2)-N(1)	1.353(3)
C(5)-O(2)	1.337(3)	C(2)-C(3)	1.371(3)
O(2)-Si(2)	1.6951(16)	C(3)-C(5)	1.406(3)
C(1)-N(1)	1.327(3)	C(5)-N(2)	1.327(3)

Table 2.4: Selected bond angles (°) for bis-(trimethylsilyl)thymine (1)

C(1)-O(1)-Si(1)	125.40(14)	C(5)-C(3)-C(2)	114.5(2)
C(1)-N(1)-C(2)	114.85(19)	N(2)-C(5)-O(2)	118.28(19)
C(1)-N(2)-C(5)	115.63(18)	N(2)-C(5)-C(3)	123.5(2)
N(1)-C(1)-O(1)	118.24(18)	C(3)-C(5)-O(2)	118.3(2)
N(1)-C(1)-N(2)	127.29(19)	N(1)-C(2)-C(3)	124.1(2)
N(2)-C(1)-O(1)	114.47(19)	C(4)-C(3)-C(5)	121.9(2)
C(5)-O(2)-Si(2)	125.46(14)	C(2)-C(3)-C(4)	123.6(2)

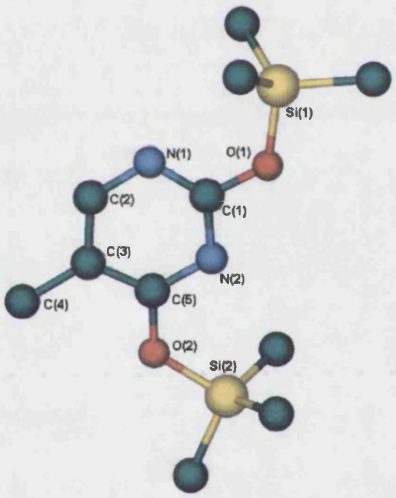


Fig 2.3 Molecular structure of 1

2.4 Structure of bis-(trimethylsilyl)cytosine (2)

Thin, needle-like crystals of **2** were formed spontaneously from a molten sample as it cooled. The molecular structure of **2** is illustrated in **Figs. 2.4 – 2.6**. Selected bond lengths and angles are presented in **Tables 2.5** and **2.6**. Crystal structure data are presented in **Appendix 8.3**.

The asymmetric unit of the crystal is formed of two molecules of **2**, held together by an N-H---N hydrogen bond. The $SiMe_3$ groups have protected the ketone and primary amine

groups, with the Si atoms in the plane of the six-membered ring, as in **1**. The Si-N [Si(1)-N(1) 1.749(3) Å, Si(4)-N(4) 1.744(2) Å] and Si-O bond lengths [Si(2)-O(1) 1.667(2) Å, Si(3)-O(2) 1.678(2) Å] compare well with the length of Si-N bonds in known compounds such as N-(2-Phenoxyphenyl)-N-(trimethylsilyl)amine [Si-N 1.745(1) Å][12], but are slightly longer than known examples of some Si-O bonds[8-10], e.g. in *hexa*-(trimethylsiloxy)benzene [Si-O 1.655(3) Å].[10] The Si-O bond distance is slightly shorter than those found in **1** (1.6906(16) Å, 1.6951(16) Å), suggesting a stronger interaction between the $SiMe_3$ group and the lone oxygen of cytosine than with the two available sites on thymine. The aromatisation of the ring has also caused significant shortening of some of the bonds in the ring [N(2)-C(4) 1.337(4) Å, C(4)-N(3) 1.322(4) Å] compared to the corresponding bonds in the unaromatised 1-methylcytosine [N(2)-C(4) 1.358(2) Å, C(4)-N(3) 1.395(2) Å][13] and cytosine [N(2)-C(4) 1.364(3) Å, C(4)-N(3) 1.374(3) Å].[14]

The bulk of the $SiMe_3$ groups has caused the C-O-Si and C-N-Si bond angles to widen from the tetrahedral [C(4)-O(2)-Si(2) 133.40(18)°, C(1)-N(1)-Si(1) 131.7(2)°] to accommodate them, though to a greater degree than in **1** in both cases. In the case of the C-O-Si bond angle, this may well be due to the relative shortness of the Si-O bond compared with **1** creating greater steric hindrance between the protecting group and the ring, and causing the band angle to widen to provide greater relief.

The molecule forms a helical polymeric chain (**Fig.2.5**) with a pitch of 21.7 Å (compared to 34 Å in β-DNA),[15] interacting *via* alternating straight N-H---O [2.26(3) Å] and N-H---N [2.24(3) Å] hydrogen bonds [N(1)-H(1)---O(2) 173.85(10)°, N(4)-H(4)---N(3) 168.08(10)°], of slightly longer length to hydrogen bonds in other cytosine compounds[13, 16-19] such as 1-methylcytosine [H(1)---O(2) 2.04(2) Å, H(4)---N(3) 2.14(2) Å].[13] The pitch involves a four molecule turn (**Fig.2.6**).

Table 2.5: Selected bond lengths (Å) for bis-(trimethylsilyl)cytosine (2)

Molecule 1		Molecule 2	
Si(1)-N(1)	1.749(3)	Si(4)-N(4)	1.744(2)
C(1)-N(1)	1.358(4)	C(5)-N(4)	1.354(4)
Si(2)-O(1)	1.667(2)	Si(3)-O(2)	1.677(2)
C(4)-O(1)	1.348(3)	C(8)-O(2)	1.362(3)
N(1)-H(1)	0.88(1)	N(4)-H(4)	0.88(1)
H(1)···O(2)	2.26(3)	H(4)···N(3)	2.24(3)

Table 2.6: Selected bond angles (°) for bis-(trimethylsilyl)cytosine (2)

Molecule 1		Molecule 2	
C(1)-N(1)-Si(1)	131.7(2)	C(5)-N(4)-Si(4)	129.9(2)
C(1)-N(1)-H(1)	109(2)	C(5)-N(4)-H(4)	117.9(2)
Si(1)-N(1)-H(1)	119(2)	Si(4)-N(4)-H(4)	111(2)
N(1)-C(1)-N(2)	119(2)	N(5)-C(5)-N(4)	118.1(2)
C(4)-O(1)-Si(2)	133.40(18)	C(8)-O(2)-Si(3)	128.37(19)
N(2)-C(4)-O(1)	118.3(2)	N(5)-C(8)-O(2)	116.9(2)
N(3)-C(4)-O(1)	113.0(2)	N(6)-C(8)-O(2)	113.8(3)
N(2)-C(4)-N(3)	128.7(3)	N(5)-C(8)-N(6)	129.3(3)
C(1)-N(2)-C(4)	115.4(2)	C(5)-N(5)-C(8)	115.5(2)
N(1)-H(1)---O(2)	173.85(10)	N(4)-H(4)---N(3)	168.08(10)

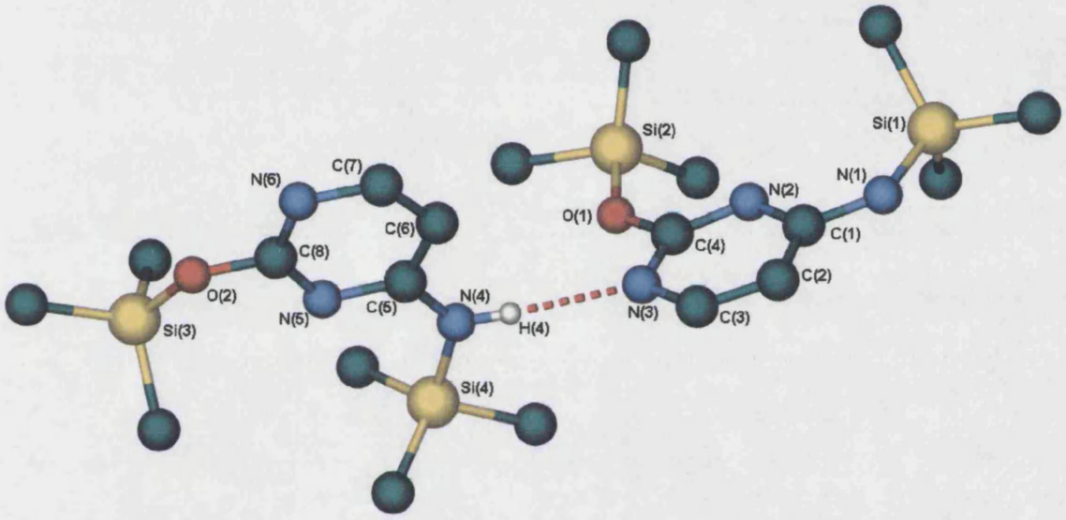


Fig 2.4 Molecular structure of the unit cell of 2

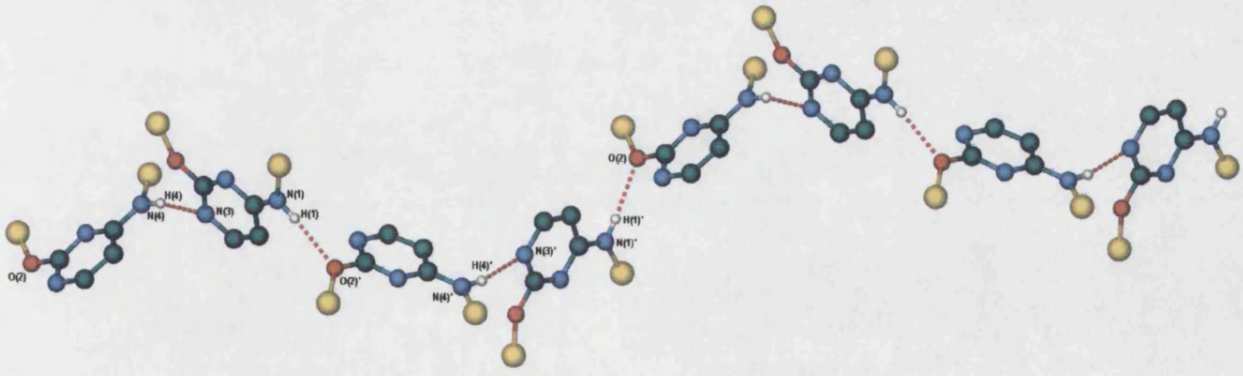


Fig.2.5 Helical structure of 2. Symmetry operator 3/2-X, 1-Y, ½+Z.

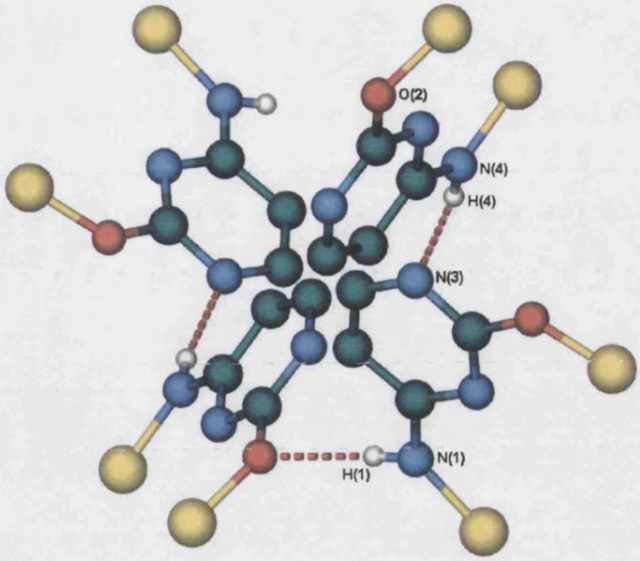


Fig.2.6 A view of 2 showing four molecule pitch of the helical chain

2.5 Structure of bis-(trimethylsilyl)adenine (3)

Thin, needle-like crystals of **3** were grown from a saturated solution of **3** in HMDS. The molecular structure of **3** is illustrated in Figs. **2.7** and **2.8**. Selected bond lengths and angles are presented in Tables **2.7** and **2.8**. Crystal structure data are presented in **Appendix 8.4**.

The two $SiMe_3$ groups have protected the primary [N(1)-Si(1) 1.750(2) Å] and secondary [N(5)-Si(2) 1.794(2) Å] exocyclic amine groups, with the Si atoms in the plane of the purine ring. The Si-N bond length in the protected primary amine compares well with that of **2** (1.749(3) Å) and other similar Si-N bonds such as in N-(2-Phenoxyphenyl)-N-(trimethylsilyl)amine [Si-N 1.745(1) Å].[12] The Si-N length in the protected secondary amine is long compared to that of known compounds such as chloro-3-(N-(tri-isopropylsilyl)pyrrole)-mercury [Si-N 1.775(2) Å].[20] This may be due in part to the silyl protecting group on the secondary amine having no bonds it can distort in order to relieve strain, and so lengthening in order to accommodate the steric bulk of the silyl group as much as possible.

The steric bulk of the $SiMe_3$ group protecting the primary amine causes the C-NH-Si moiety to deform slightly to accommodate a wide C-N-Si bond [C(1)-N(1)-Si(1) 127.25(19)°] compared with the corresponding C-N-H bond in 9-methyladenine [C(1)-N(1)-H(1) 120.2(1)°].[21]

The molecule forms a dimer held together by two symmetry-related N-H---N hydrogen bonds [N(1)-H(1)---N(4) 2.38(1) Å] [N(1)-H(1)---N(4) 169.48(5)°]. These are longer than the N-H---N hydrogen bonds founds in **2** (2.26(3) Å, 2.24(3) Å), and 1-methylcytosine (2.14(2) Å).[13]

The bulk of the $SiMe_3$ groups protecting the amines is also the driving force behind the orientation of the molecules within the dimer. The planes of the two adenine molecules lie approximately perpendicular to each other (**Fig 2.8**), orientating the $SiMe_3$ groups as far from each other as possible.

Table 2.7: Selected bond lengths (Å) for bis-(trimethylsilyl)adenine (3)

Si(1)-N(1)	1.750(2)	C(1)-C(3)	1.393(3)
C(1)-N(1)	1.365(3)	C(1)-N(2)	1.347(3)
Si(2)-N(5)	1.794(2)	C(3)-C(4)	1.382(3)
C(4)-N(5)	1.384(3)	N(1)-H(1)	0.80(3)
C(5)-N(5)	1.380(3)	H(1)---N(4)	2.380(5)

Table 2.8: Selected bond angles (°) for bis-(trimethylsilyl)adenine (3)

C(1)-N(1)-Si(1)	127.25(19)	C(4)-N(5)-C(5)	103.82(19)
C(1)-N(1)-H(1)	114.0(19)	C(1)-C(3)-C(4)	117.4(2)
Si(1)-N(1)-H(1)	118.2(19)	C(1)-C(3)-N(4)	132.0(2)
N(1)-C(1)-N(2)	118.7(2)	N(4)-C(5)-N(5)	115.4(2)
N(1)-C(1)-C(3)	123.0(2)	N(5)-C(4)-C(3)	107.0(2)
N(2)-C(1)-C(3)	118.2(2)	N(1)-H(1)---N(4)	169.48(5)
C(4)-N(5)-Si(2)	127.05(16)	C(5)-N(4)---H(1)	133.02(5)
C(5)-N(5)-Si(2)	128.80(17)	C(3)-N(4)---H(1)	112.56(5)

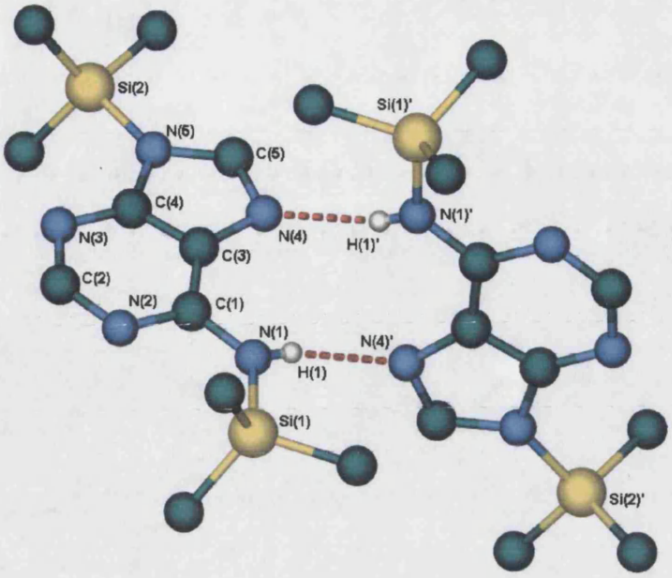


Fig.2.7. Molecular structure of 3. Symmetry operator 1-X, Y, ½-Z.

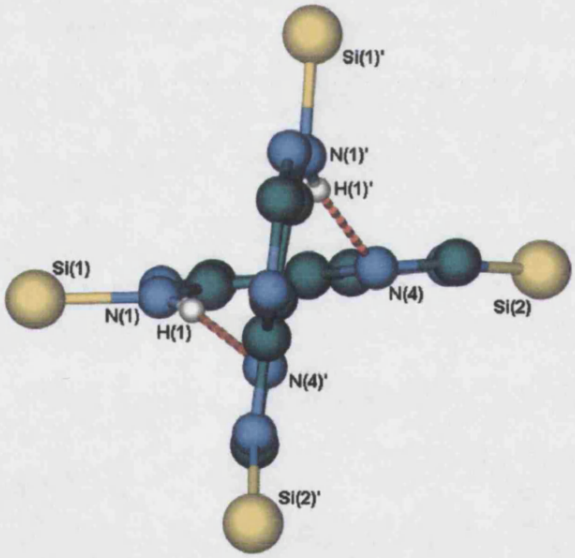


Fig 2.8. Perpendicularity of dimer molecules in 3

2.6 Structure of tris-(trimethylsilyl)guanine (4)

Crystals of **4** were grown from a saturated solution of **4** in HMDS. The molecular structure of **4** is illustrated in **Figs. 2.9 – 2.11**. Selected bond lengths and angles are presented in **Tables 2.9** and **2.10**. Crystal structure data are presented in **Appendix 8.5**.

The three $SiMe_3$ groups have protected the primary [N(4)-Si(3) 1.740(4) Å] and secondary [N(2)-Si(2) 1.778(4) Å] amine groups, and the carbonyl group [O(1)-Si(1) 1.665(4) Å], with the Si atoms in the plane of the purine rings, as in the structure of **3**. The Si-O distance is compares well with Si-O bond distances in similar silyl ethers[8-10] such as *hexa*-(trimethylsiloxy)benzene [Si-O 1.655(3) Å][10] and **2** (1.667(2) Å), though is shorter than the Si-O distances in **1** (1.6906(16) Å, 1.6951(16) Å). The Si-N distance in the primary amine compares well with **2** (1.749(3) Å), **3** (1.750(2) Å) and known compounds such as N-(2-Phenoxyphenyl)-N-(trimethylsilyl)amine [Si-N 1.745(1) Å].[12] The Si-N distance in the secondary amine compares well with similar systems, such as chloro-3-(N-(tri-isopropylsilyl)pyrrole)-mercury [Si-N 1.775(2) Å].[20]

The bulk of the $SiMe_3$ groups is evident in the distortion of the moieties two of them protect. The C-O-Si bond widens significantly past 120° to accommodate the protecting group [C(1)-O(1)-Si(1) 129.3(3)°], and the primary amine group is straightened about the C-NH-Si bond for the same reason [C(5)-N(4)-Si(3) 128.1(4)°]. The third $SiMe_3$ group, on the secondary amine, is unable to distort the bond angles around it and may extend in order to relieve steric strain.

The molecule forms a polymeric structure held together by bent C-H---N hydrogen bonds [C(3)-H(3)---N(1) 2.466(5) Å] [C(3)-N(1)---H(3) 145.15(5)°], forming a zig-zag chain (**Fig.2.10**). This orientation is probably adopted on steric grounds to keep the $SiMe_3$ groups as far from each other as possible (**Fig.2.11**), as in **3**. The formation of hydrogen bonds between nitrogen and a relatively unpolarised proton attached to carbon is surprising, due to the presence of an available N-H on the protected primary amine, but not unknown. The history of C-H---O hydrogen bonds and their use in crystal engineering has been recently reviewed,[22] and comparison of the C-H---N hydrogen bond in **4** with a range of known examples of C-H---N bonds [C-H---N 2.44-2.98][23] suggests they are strong for this type of interaction, though compare well with some of the shorter interactions, such as in methylpyrazine [C-H---N 2.44(2)-2.76(2) Å][23]. The sum of the van der Waals radii of H and N is 2.75 Å,[24] so the C-H---N bond length of 2.446(5) Å in **4** suggests intermolecular interaction. It is possible that the molecule is driven to adopt this arrangement of hydrogen bonding on steric grounds, as the

formation of more expected N(4)-H(4)---N(1) hydrogen bonds would bring the silyl groups into closer proximity with each other and place greater strain on the molecule.

Table 2.9: Selected bond lengths (Å) for tris-(trimethylsilyl)guanine (4)

Si(1)-O(1)	1.665(4)	Si(3)-N(4)	1.740(4)
C(1)-O(1)	1.334(5)	C(5)-N(4)	1.380(6)
C(1)-C(2)	1.381(5)	C(5)-N(3)	1.313(6)
C(1)-N(5)	1.329(6)	C(5)-N(5)	1.353(6)
Si(2)-N(2)	1.778(4)	C(3)-N(1)	1.316(7)
N(2)-C(3)	1.358(7)	C(3)-H(3)	0.95(1)
N(2)-C(4)	1.384(7)	H(3)---N(1)	2.466(5)

Table 2.10: Selected bond angles (°) for tris-(trimethylsilyl)guanine (4)

Si(1)-O(1)-C(1)	129.3(3)	N(3)-C(5)-N(4)	116.5(4)
C(2)-C(1)-O(1)	119.9(4)	N(5)-C(5)-N(4)	114.8(4)
N(5)-C(1)-O(1)	119.7(4)	N(3)-C(5)-N(5)	128.7(4)
C(2)-C(1)-N(5)	120.4(4)	N(1)-C(3)-H(3)	122.43(5)
Si(2)-N(2)-C(3)	126.8(4)	N(2)-C(3)-H(3)	122.43(5)
Si(2)-N(2)-C(4)	128.5(3)	C(3)-H(3)---N(1)	140.95(5)
C(3)-N(2)-C(4)	104.4(4)	C(3)-N(1)---H(3)	145.15(5)
Si(3)-N(4)-C(5)	128.1(4)	C(2)-N(1)---H(3)	101.1(1)

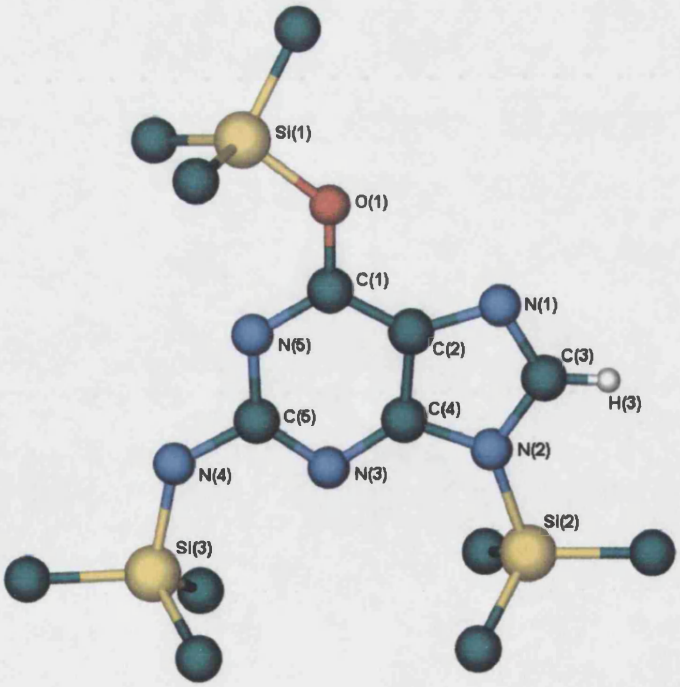


Fig 2.9 Molecular Structure of 4

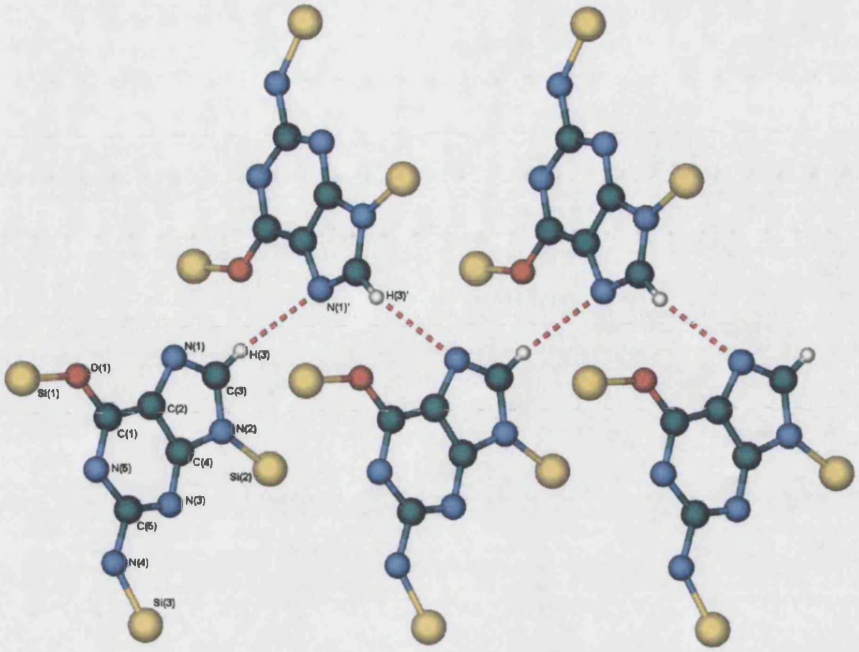


Fig.2.10. Zigzag chain structure of 4 . Symmetry operator 3/2-X, Y-½, ½-Z.

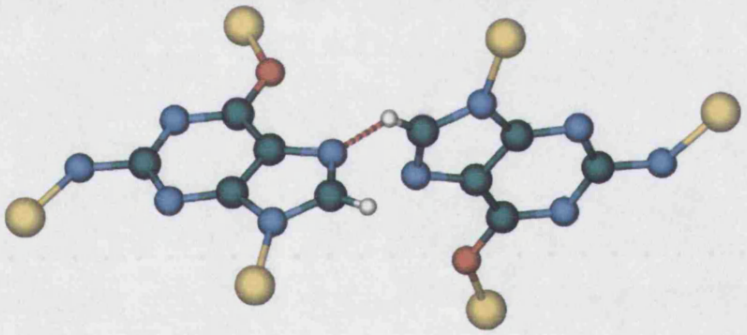


Fig 2.11. A view of 4 showing maximum separation of silyl groups

2.7 Conclusions

Crystalline samples of bis-(trimethylsilyl)thymine (**1**), bis-(trimethylsilyl)cytosine (**2**), bis-(trimethylsilyl)adenine (**3**) and tris-(trimethylsilyl)guanine (**4**) have been grown, and structurally characterised by X-ray diffraction. Each showed different structural interactions in the solid state. **1** was shown to be a monomer in the solid state, having no free protons for intermolecular interaction, **2** forms a polymeric chain *via* alternating N-H---O and N-H---N hydrogen bonds, **3** forms a dimer *via* two N-H---N hydrogen bonds, and **4** forms a polymeric chain *via* unexpected C-H---N hydrogen bonds.

2.8 Experimental

2.2 Synthesis of bis-(trimethylsilyl) DNA bases (1-4)

A mixture of HMDS, the DNA base in question and a few crystals of ammonium sulphate was refluxed until the opacity of the mixture due to the suspended base had cleared. The excess HMDS was then removed under reduced pressure. Data for the amounts of reactants used is presented in **Table 2.11**.

Table 2.11: Reactant amounts and reaction times for the synthesis of 1-4

	Base Amount		HMDS Amount		
	g	mmol	cm^3	mmol	Reaction Time (h)
Thymine	10.4	82	20.0	94	20
Cytosine	5.0	45	28.5	135	20
Adenine	5.0	37	35.0	160	72
Guanine	5.0	33	21.0	99	144

In the case of thymine, the reaction afforded a pale colourless liquid that spontaneously crystallised into the solid bis-(trimethylsilyl)thymine **1** (20.64 g, 93 %).

In the cases of cytosine, adenine and guanine, the reactions afforded crude solids that were distilled under vacuum (1 mm Hg). The distillations each yielded two products, the first distilling at *ca.* 60°C and being found to be excess HMDS, the second a colourless oil which solidified on cooling, found to be the silylated product. Pertinent data to the distillations are presented in **Table 2.12**.

Table 2.12: Distillation data for 2-4

			Yield	
	Crude Product	**Distillation Temp (°C)**	g	%
2	White Solid	200	1.59	20
3	Yellow Solid	240	5.21	50
4	Yellow Solid	250	8.34	72

2.9 References

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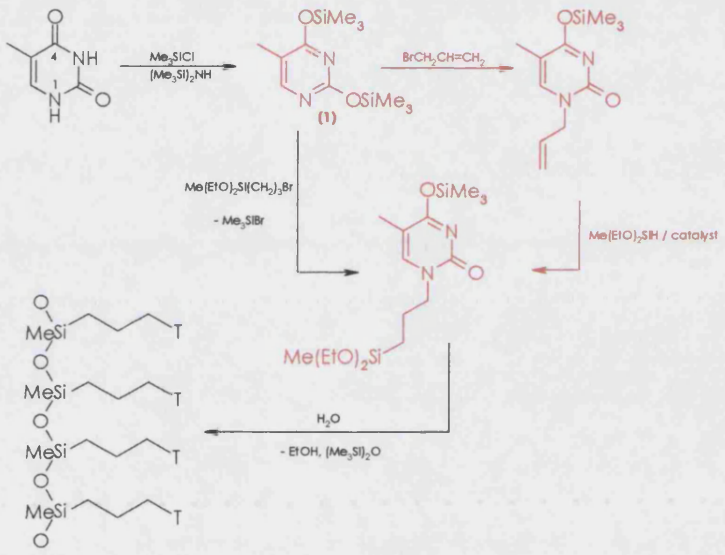
Chapter 3

Formation of alkenyl DNA bases

3.1 Introduction

Bis-(trimethylsilyl)thymine (**1**) can be developed in two ways to generate a hydrolysable precursor to the desired siloxane polymers, either by introduction of an alkenyl group in place of the protecting group followed by hydrosilylation, or by substitution of the protected base with a suitable α-silyl-ω-bromoalkane (**Scheme 3.1**). This chapter concerns the first of these two routes, substituting the silylalkyl group of the previously protected base (Chapter 2) with an olefin, and subsequent reaction with a compound containing an Si-H bond to form a DNA base with a pendant silylalkyl group. A family of alkenyl DNA base compounds available *via* a single procedure would act as potential precursors for a hydrosilylation reaction leading to the target polymer with pendant DNA bases.



Scheme 3.1

The substitution reaction of allyl bromide with bis-(trimethylsilyl)thymine (**1**) is known to produce the air stable alkenylthymine in high yield,[1] and higher homologues e.g. 1-pentenylthymine, are also known,[2] though little is reported on this species. **1** can be synthesised in high purity and quantity, so it was of interest to carry out investigations using alkenyl bromides and **1** in order to establish a simple, repeatable route to a range of 1-alkenylthymines for further reaction. It was further of interest to attempt to extend this procedure to other DNA bases, particularly adenine due to its complementary pairing with thymine.[3] As discussed in the introduction, there has been recent interest in the addition of olefins to DNA bases *via* various different methods, such as solid-liquid phase transfer

catalysis,[4] and alkenylation using acetylolefins catalysed by palladium catalysts,[5] though there has been little systematic investigation of the properties and chemistry of a range of these types of molecules synthesised by the same method.

In order to carry out an effective hydrosilylation, it is also preferable to protect the 1-alkenylthymine with a sufficiently bulky group at the 3-position, in order to inhibit the reaction taking place at anywhere but the sterically uncrowded terminal alkene. The method used to protect thymine to form **1**, involving HMDS and dimethylsulfate, can be used with the 1-alkenylthymine to add a trimethylsilylgroup to the carbonyl group in the 4-position. The hydrosilylation step will ideally produce a silylalkyl DNA base in reproducibly high yield, with physically different by-products that are easily removed during the synthesis. A silyl group with sufficient steric bulk to direct the addition to form terminal silylalkanes as opposed to branched products is ideal. Phenyldimethylsilane is a commonly available compound with considerable steric bulk that could direct the synthesis in the desired manner.

This chapter describes a general procedure for the synthesis of 1-alkenylthymines previously synthesised by other methods, and extension of this methodology to other bases. It also describes the reprotection of 1-allylthymine with HMDS to form (trimethylsilyl)-1-allylthymine, and the reaction of a similarly protected sample of 1-butenylthymine with phenyldimethylsilane.

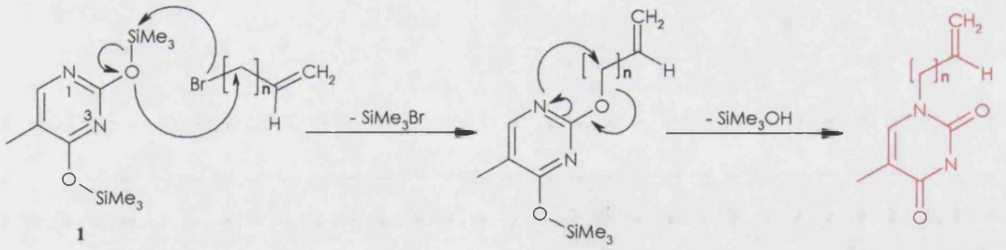
3.2 Synthesis of 1-alkenylthymines

A THF solution of bis-(trimethylsilyl)thymine (**1**) and an excess of alkenyl bromide were refluxed until the IR spectrum of the reaction mixture displayed no further generation of the product, measured by monitoring the evolution of a peak at 1720 cm^{-1} due to the carbonyl group in thymine. After removal of the volatiles, thick liquids remained, purified either by recrystallisation or column chromatography on silica followed by recrystallisation, yielding an air stable, neutral product in each case. Pertinent reaction and physical data are presented in **Table 3.1**.

Table 3.1: Reaction data for synthesis of 1-alkenylthymines

	Alkenyl Bromide	Reaction Time (h)	Yield (%)	Appearance	Melting Point (°C)
5	Allyl bromide	72	81	White platelets	109-11[a]
6	4-bromo-1-butene	72	59	White platelets	119-21
7	5-bromo-1-pentene	144	18	Brown needles	134-6

[a] *Lit* 112°C[1]



Possible reaction mechanism in the alkenylation of 1

It is expected that the reaction proceeds *via* a transitional kinetic product, the bromide displacing the $SiMe_3$ group and forming an alkenyl ether. This undergoes subsequent internal rearrangement to form a thermodynamic product with a carbonyl group and the alkenyl moiety directly attached to the nitrogen on the ring. Steric factors dictate the regiochemistry of the reaction, the bulk of the $SiMe_3$ groups hindering the nitrogen in the 3-position and directing the substitution to the less hindered 1-position. The remaining silyl ether then hydrolyses in air to liberate the free 1-alkenylthymine. The ^1H NMR spectrum of **5** compares well with the literature,[1] and those of **6** and **7** display significant similarities to both each other and that of **5**. Comparable resonances between the three compounds are presented in **Table 3.2**

Table 3.2: ^1H NMR data (ppm) for 1-alkenylthymines

	5	**6**	**7**
C-C*H*$_3$ (s, 3H)	1.91	1.92	1.92
C$_{ar}$-*H* (s, 1H)	7.08	6.98	6.98
N-*H* (bs, 1H)	10.65	9.68	9.84
C$_{vinyl}$-*H* (m, 1H)	5.87	5.76	5.79
CH=C*H*$_2$ (m, 2H)	5.26	5.10	5.05
N-C$_\alpha$*H*$_2$	4.35 (d, J = 5.6 Hz)	3.78 (t, J = 7.0 Hz)	3.71 (t, J = 7.3 Hz)
C$_\beta$*H*$_2$		2.47 (m)	2.11 (m)
C$_\gamma$*H*$_2$			1.80 (m)

The $\delta(^1H)$ for the α-methylene protons in **5** compares well to other examples of allyl methylene groups bonded to aromatic nitrogen atoms, such as in 1-allylimidazole [N-C*H*$_2$ 4.50 ppm (d, J = 5.6 HZ)].[6] The peaks due to the β- and γ-methylene protons in **6** and **7** appear as apparent pentuplets due to multiple couplings with adjacent protons.

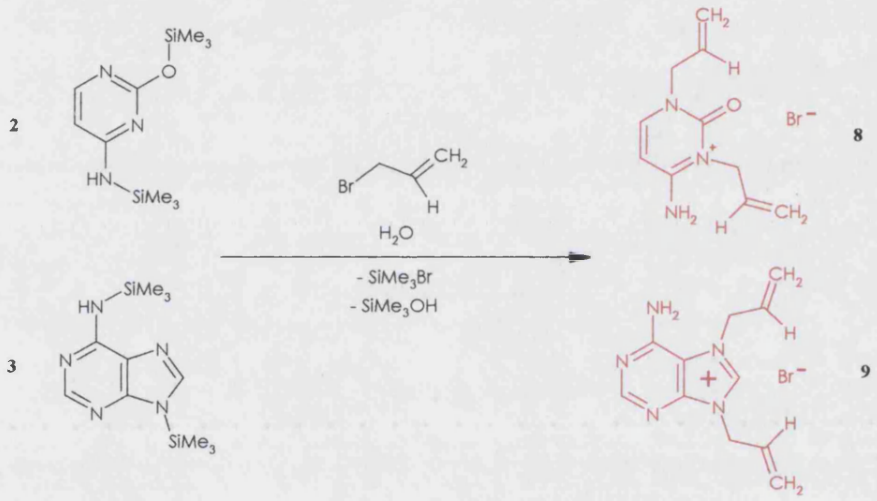
The $^{13}C\{^1H\}$ NMR spectrum of **5** once again compared well with the literature values,[1] and bears similarities to comparable resonances in **6** and **7**, presented in **Table 3.3**.

Table 3.3: $^{13}C\{^1H\}$ NMR data (ppm) for 1-alkenylthymines

	5	6	7
C-CH_3	12.3	12.3	12.3
C_{vinyl}-H	118.9	118.5	115.8
CH=CH_2	131.9	133.5	136.9
N-$C_\alpha H_2$	49.8	48.0	48.0
$C_\beta H_2$		33.3	30.4
$C_\gamma H_2$			28.0

3.3 Reaction of other bis-(trimethylsilyl) DNA bases with allyl bromide

THF solutions of bis-(trimethylsilyl)cytosine (**2**) and bis-(trimethylsilyl)adenine (**3**) and an excess of allyl bromide were refluxed for 72 h, after which immiscible oils were formed.



After removal of the volatiles, thick oily residues remained. In the case of the reaction involving **2**, purification was by direct recrystallisation from chloroform solution, yielding the product 1,3-bis-allylcytosinium bromide (**8**) as air stable white crystals, soluble only in DMSO post recovery. The product from the reaction involving **3** was purified by direct recrystallisation from a three-time filtered chloroform solution, yielding the product 7,9-bis(allyl)adeninium bromide hydrate (**9**) as air stable, very sparingly soluble orange crystals in low yield, resulting in part from the recovery process of the crystals. Pertinent reaction and physical data are presented in **Table 3.4**

Table 3.4: Reaction data for the allylation of protected DNA bases

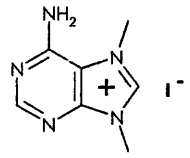
	Protected Base	Crude Product Colour	Yield (%)	Melting Point (°C)
8	Cytosine	Yellow	9	224-226
9	Adenine	Orange-brown	4	112-113

The bis-allylation of **2** and **3** was unexpected, and is probably due to the excess of allyl bromide used in the reaction. An excess of allyl bromide was used as in the formation of 1-allylthymine (**5**), and it was assumed a similar monoallylation would take place with cytosine and adenine. In both cases, the yield is very low, and it could be assumed that the recovered products are minor to another, unrecovered species. However, the thin layer chromatography of the crude reactions mixtures showed only spots corresponding to the starting materials and the single product. It must be assumed that the bis-allylated product was produced in low yield as the main product.

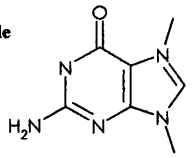
In the case of **8**, the bromide has probably reacted first with the protected ketone in **2** in the 2-position and eliminated trimethylsilylbromide, before undergoing internal rearrangement and forming an N-substituted product, in the same manner as in the formation of 1-allylthymine (**5**). However, a further molecule of allyl bromide has reacted with the 1-allylcytosine. The second allylation has not occurred at the exocyclic amine and eliminated a second molecule of trimethylsilylbromide, as the bromide ion remains in the molecule as a counterion to a positively charged fragment formed in the reaction. Instead of replacing the silyl group, it appears that the second molecule of allyl bromide is subject to direct attack from the lone pair on the heterocyclic nitrogen atom in the 3-position, while the silyl group undergoes hydrolysis and is eliminated as trimethylsilanol.

In the case of **9**, it is likely that the first allylation takes place at the 9-position, the most basic of the nitrogen sites in adenine (N9 >> N7 >> N1),[7] eliminating trimethylsilylbromide. However, rather than reacting a second time at the 1-position and eliminating further trimethylsilylbromide, reaction takes place at the 7-position with the lone pair on the heterocyclic nitrogen atom, retaining the bromide in the molecule. The second protecting group is eliminated as trimethylsilanol *via* hydrolysis. The relative basicity of the nitrogen atoms in adenine may take precedence over steric factors in dictating the regiochemistry of the reaction, directing the allylation to take place at the most basic of the remaining sites rather than the sterically unhindered primary amine.

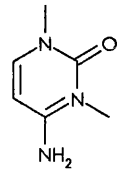
Other examples of bis-substituted DNA bases are known, both as neutral compounds and with halide counterions. 7,9-dimethyladenine hydroiodide was formed from a substituted imidazole in a ring forming reaction,[8] and 7,9-dimethylguanine[9] and 1,3-dimethylcytosine[10] were formed by reaction of the base in question with dimethylsulphate in dimethylformamide. 1,3-dimethylcytosinium is also known to support iodide[11] and chloride[12] counterions.



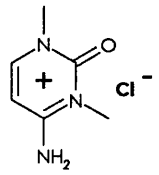
7,9-dimethyladenine hydroiodide



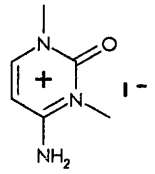
7,9-dimethylguanine



3-dimethylcytosine



1,3-dimethylcytosinium chloride



1,3-dimethylcytosinium iodide

H and $^{13}C\{^1H\}$ NMR data for the allyl moieties in **8** and **9** are presented in **Tables 3.5** and **3.6**.

Table 3.5: ^1H NMR data (ppm) for bis-(allyl) DNA bases

	8	**9**
N-$C_\alpha H_2$	4.46 (d, 2H, J = 5.0 Hz) 4.60 (d, 2H, J = 5.0 Hz)	Not Observed
C_{vinyl}-H (m, 1H)	5.88	5.88
CH=CH_2 (m, 2H)	5.22	5.21

Table 3.6: $^{13}C\{^1H\}$ NMR data (ppm) for bis-(allyl) DNA bases

	8	**9**
N-$C_\alpha H_2$	45.3 51.6	Not Observed
C_{vinyl}-H	117.0 118.2	119.3 119.9
CH=CH_2	129.2 131.7	130.7 131.6

In both cases, the position of the terminal alkenyl and vinyl peaks compares well to that of **5** and similar compounds such as 1-allylimidazole [$\delta(^1H)$ C_{vinyl}-H (m) 5.91, CH=CH_2 (m) 5.18 ppm].[6]

In the case of **8**, the position of the resonances due to the methylene protons in the ^1H NMR is considerably further downfield than the relative peak in **5**, though compares well with the methylene group in 1-allylimidazole [N-CH_2 (d) 4.50 ppm].[6] In addition to those in the table, the spectrum of **8** also displays doublets (J = 8.0 Hz) at δ = 6.20 and 7.98 ppm, assigned to the two protons attached to the heterocyclic ring, both considerably further downfield than those found in **2** [δ = 5.56, 7.73 ppm]. In the $^{13}C\{^1H\}$ NMR spectrum, in addition to those in **Table 3.6**, peaks at δ = 94.1, 147.1, 147.7 and 158.6 ppm were assigned to the carbons in the heterocyclic ring.

In the case of **9**, the poor resolution of the peaks is probably due to the extremely poor solubility of **9** in available solvents, and the inequivalency of the allyl groups producing overlapping resonances. No peaks are observed for the methylene protons on the allyl moieties in the ^1H NMR spectrum, probably as a result of the poor resolution of the spectrum, but the $^{13}C\{^1H\}$ NMR spectrum displays resonances at δ = 140.0, 148.4, 151.5 and 155.5 ppm, assigned to four of the five carbons in the heterocyclic ring on comparison with the corresponding peaks found in the spectrum of adenine.[13] A peak corresponding to the fifth, at approximately δ = 118.5 ppm, was not observed, and may be obscured by the peaks assigned to the vinyl carbons on the allyl moieties, as vinyl carbon peaks occur in similar positions in the $^{13}C\{^1H\}$ NMR spectra of similar compounds, such as 1-allylthymine (**5**) [δ = 118.9 ppm].

3.4 Structure of 1,3-bisallylcytosinium bromide (8)

Tabular white crystals of **8** were grown from a saturated solution of the reaction mixture in chloroform. The molecular structure of **8** is illustrated in **Figs.3.1** and **3.2**. Selected bond lengths and angles are presented in **Tables 3.7** and **3.8**. Crystallographic data is presented in **Appendix 8.6**.

The asymmetric unit of the crystal is formed of a single molecule of **8**, which interacts with itself *via* two symmetry-related hydrogen bonds to the bromide counterion. The two allyl groups have added to the heterocyclic ring in the 1- [N(3)-C(8) 1.475(6) Å] and 3- [N(2)-C(5) 1.479(6) Å] positions. The bond lengths in the allyl moieties compare well with those in 9-allyladeninium chloride hydrate [N-C_α 1.474 Å, C_α-C_β 1.490 Å, C_β-C_γ 1.292 Å].[14] The heterocyclic ring has distorted slightly to accommodate the two allyl moieties, the C(2)-

N(4) bond [1.407(6) Å] lengthened relative to the analogous bond in 1-methylcytosine [N(2)-C(4) 1.358(2) Å][15] and cytosine [N(2)-C(4) 1.364(3) Å].[16]

The bond angles in the two allyl moieties [N(3)-C(8)-C(9) 112.2(5)°, C(8)-C(9)-C(10) 127.3(5)°; N(2)-C(5)-C(6) 113.4(5)°, C(5)-C(6)-C(7) 127.2(5)°] compare well with those in **9**, though similar compounds such as 9-allyladeninium chloride hydrate [N-C_α-C_β 109.1° C_α-C_β-C_γ 123.7°][14] show a different geometry, with a more acute angle about the α-carbon and a more obtuse angle about the β-carbon moiety than in **8**.

The molecule forms a dimer *via* two symmetry-related hydrogen bonds to the bromide counterion [N(1)-H(1A)---Br 2.491(6) Å, 152.3°], [N(1)-H(1B)---Br 2.412(6) Å, 172.8°], and forms an extended structure *via* much weaker interactions between the bromide counterion and the 1-allyl moiety [C(8)-H(8B)---Br 2.981 Å, 129.2°]. The extended structure is formed of ladders of dimers of **8**, held apart by the interactions of the allyl moieties, which point above the plane of the dimer in one molecule, and below in the other.

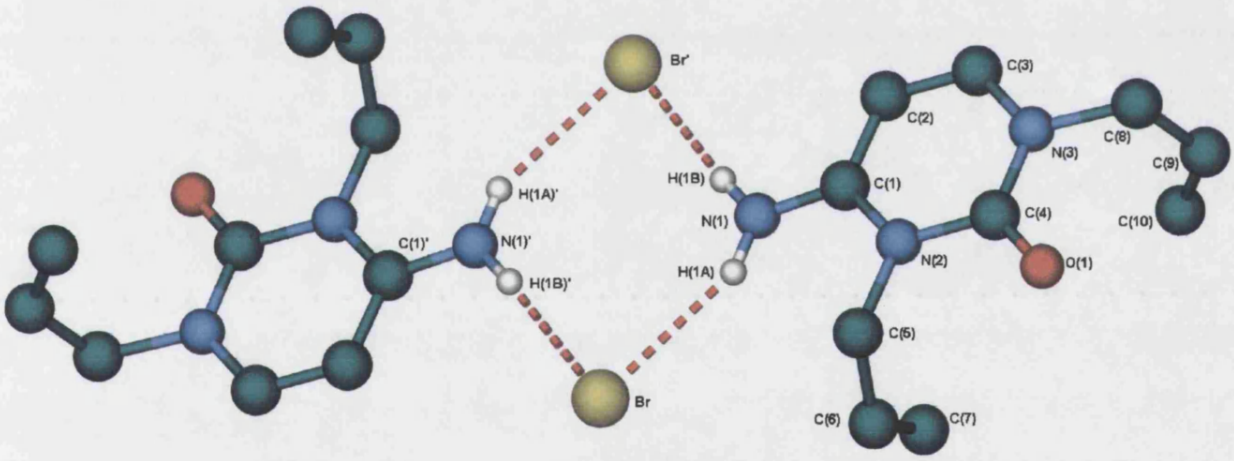


Fig.3.1 Dimeric structure of 8. Symmetry operator 2-x, 1-y, 1-z

Table 3.7: Selected bond lengths (Å) for 1,3-bisallylcytosinium bromide (8)

N(3)-C(8)	1.475(6)	N(2)-C(5)	1.479(6)
C(8)-C(9)	1.493(8)	C(5)-C(6)	1.507(8)
C(9)-C(10)	1.340(10)	C(6)-C(7)	1.315(9)
C(1)-N(1)	1.336(6)	C(4)-O(1)	1.213(6)
N(2)-C(4)	1.407(6)	N(3)-C(4)	1.375(7)
H(1A)---Br	2.491(6)	H(1B)---Br	2.412(6)
H(8B)---Br	2.891(6)		

Table 3.8: Selected bond angles (°) for 1,3-bisallylcytosinium bromide (8)

N(3)-C(8)-C(9)	112.2(5)	N(2)-C(5)-C(6)	113.4(5)
C(8)-C(9)-C(10)	127.3(5)	C(5)-C(6)-C(7)	127.2(5)
C(3)-N(3)-C(8)	119.8(4)	C(1)-N(2)-C(5)	121.3(4)
C(4)-N(3)-C(8)	118.2(4)	C(4)-N(2)-C(5)	116.4(4)
C(3)-N(3)-C(4)	121.9(4)	C(1)-N(2)-C(4)	122.3(4)
N(1)-H(1A)---Br	152.3(5)	N(1)-H(1B)---Br	172.8(5)
C(8)-H(8B)---Br	129.2(5)		

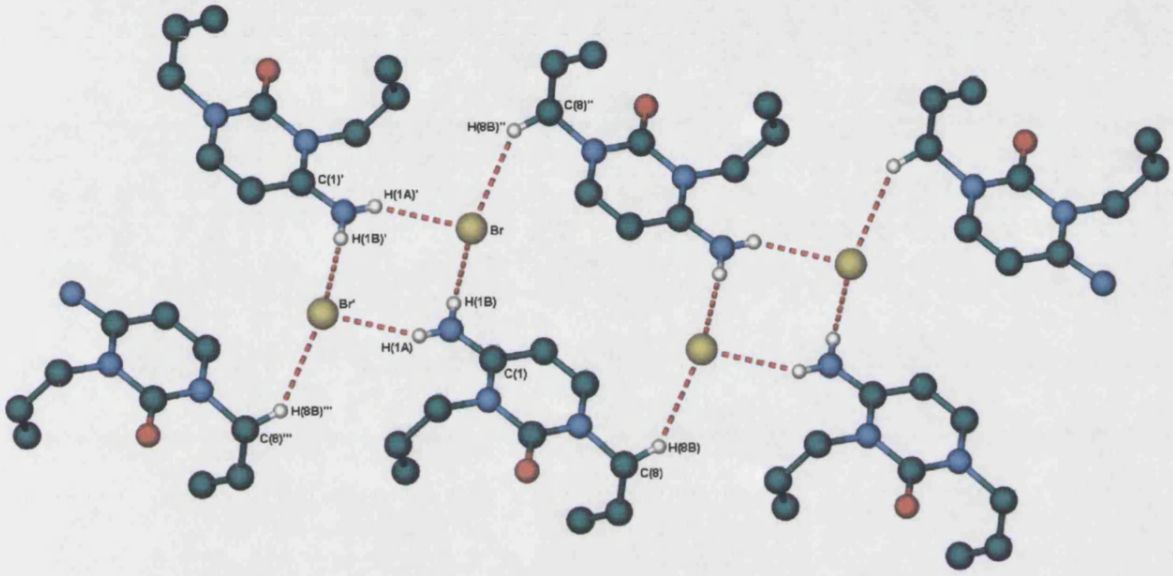


Fig.3.2 Extended structure of 8

3.5 Structure of 7,9-bis-(allyl)adeninium bromide hydrate (9)

Orange, tabular crystals of **9** were grown from saturated solution of the reaction mixture in chloroform. The molecular structure of **9** is illustrated in **Fig.3.3**. Selected bond lengths and angles are presented in **Tables 3.9** and **3.10**. Crystallographic data is presented in **Appendix 8.7**.

The asymmetric unit of the crystal is formed of two molecules of **9** with water of crystallisation, each of which dimerises *via* two symmetry related N-H---N bonds, and an extended hydrogen-bonded lattice *via* the bromide counterion and water molecule. In each case, the two allyl groups have added to the adenine molecule in the 7- [N(1)-C(6) 1.468(6) Å, N(6)-C(17) 1.473(5) Å] and 9- [N(2)-C(9) 1.477(6) Å, N(7)-C(20) 1.477(5) Å] positions, with the two moieties extending in opposite directions, up and down relative to the plane of

the heterocyclic ring as in **8**. The bond lengths in the two allyl moieties compare well with those in similar compounds, such as 9-allyladeninium chloride hydrate [N-C_α 1.474 Å, C_α-C_β 1.490 Å, C_β-C_γ 1.292 Å],[14] though one of the 9-allyl moieties in the chloride [C(7)-C(8) 1.212(7) Å] has a significantly shorter C_β-C_γ bond length than in **9**.

The bond angles in the two allyl moieties on each adenine molecule compare well with each other, and similar molecules such as 9-allyladeninium chloride hydrate [N-C_α-C_β 109.1°, C_α-C_β-C_γ 123.7°].[14]

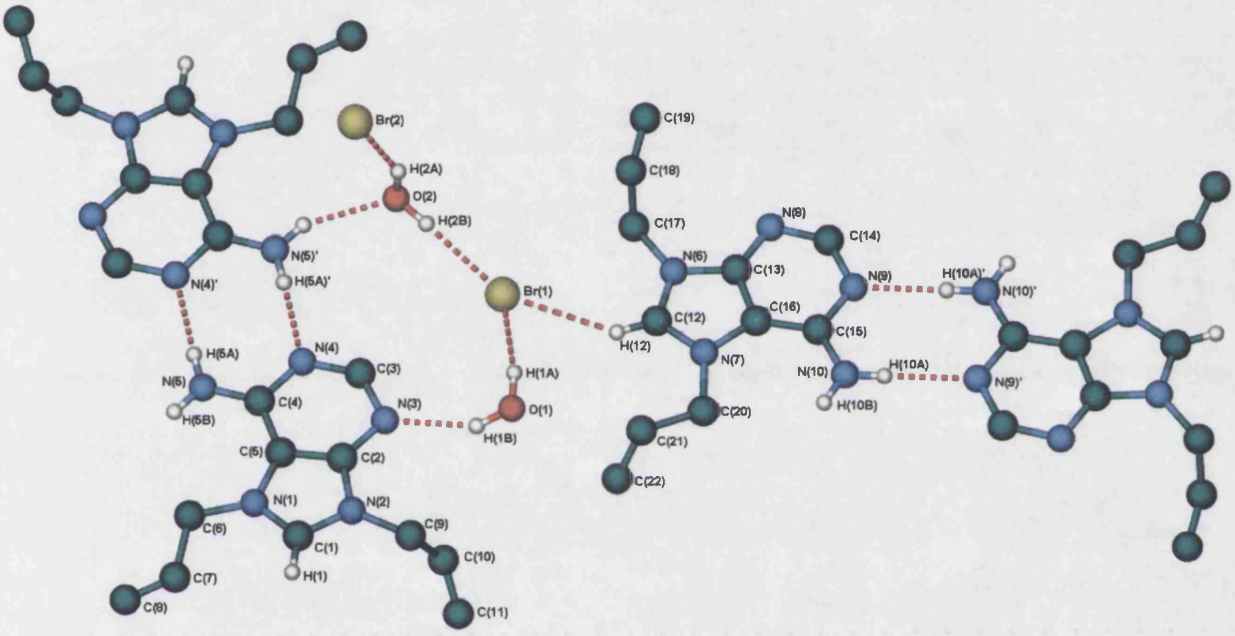


Fig.3.3 Molecular structure of 9. Symmetry operator (left) 1-x, -y, 1-z; (right) -x, -y, 3-z

Of most interest is the extensive hydrogen bonding throughout the crystal lattice. **9** forms a dimer, interacting with itself *via* two symmetry related N-H---N hydrogen bonds [N(5)-H(5A)---N(4) 2.068(5) Å, 178.2(5)°; N(10)-H(10A)---N(9) 2.078(5) Å, 178.5(5)°], shorter than those in bis-(trimethylsilyl)cytosine (**2**) [H(1)---O(2) 2.26(3) Å, H(4)---N(3) 2.24(3) Å] and bis-(trimethylsilyl)adenine (**3**) [H(1)---N(4) 2.38(1) Å]. In the case of the lattice propagation *via* the bromide and water molecules, one water molecule interacts with the asymmetric unit *via* an O-H---N bond [O(1)-H(1B)---N(3) 2.041(5) Å, 147.1(5)°], and with the bromide ion *via* an O-H---Br bond [O(1)-H(1A)---Br(1) 2.397(5) Å, 160.6(5)°]. The second water molecule interacts differently, with the asymmetric unit *via* an N-H---O bond [N(5)-H(5B)---O(2) 2.165(5) Å, 153.9(5)°], and with two bromide ions via O-H---Br bonds

[O(2)-H(2A)---Br(2) 2.503(5) Å, 151.4(5)°; O(2)-H(2B)---Br(1) 2.409 Å, 171.3(5)°]. **9** also interacts directly with the bromide ion *via* a C-H---Br bond [C(1)-H(1)---Br(2) 2.578(5) Å, 156.8(5)°; C(12)-H(12)---Br(1) 2.761(5) Å, 145.8(5)°].

Table 3.9: Selected bond lengths (Å) for 7,9-bisallyladeninium bromide hydrate (9)

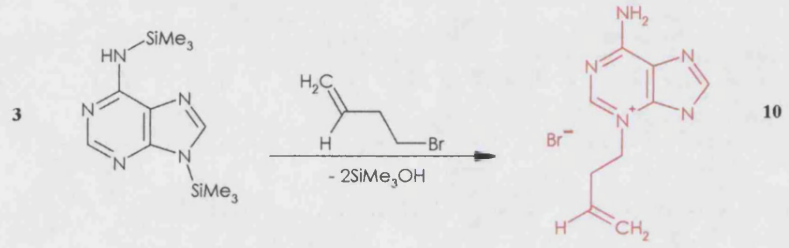
Molecule 1		Molecule 2	
N(1)-C(6)	1.468(6)	N(6)-C(17)	1.473(5)
C(6)-C(7)	1.508(7)	C(17)-C(18)	1.470(8)
C(7)-C(8)	1.212(7)	C(18)-C(19)	1.289(8)
N(2)-C(9)	1.477(6)	N(7)-C(20)	1.477(5)
C(9)-C(10)	1.469(8)	C(20)-C(21)	1.486(7)
C(10)-C(11)	1.263(10)	C(21)-C(22)	1.287(8)
C(4)-N(5)	1.413 (6)	C(15)-N(10)	1.325(5)
C(1)-H(1)	0.940(2)	C(12)-H(12)	0.940(2)
H(1)---Br(2)	2.578(5)	H(12)---Br(1)	2.761(5)
H(5A)---N(4)	2.068(5)	H(5B)---O(2)	2.165(5)
H(1A)---Br(1)	2.397(5)	H(1B)---N(3)	2.041(5)
H(2A)---Br(2)	2.503(5)	H(2B)---Br(1)	2.409(5)
H(21)---O(1)	2.513(5)		

Table 3.10: Selected bond angles (°) for 7,9-bisallyladeninium bromide hydrate (9)

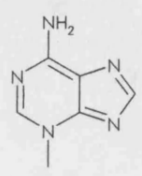
Molecule 1		Molecule 2	
N(1)-C(6)-C(7)	113.2(4)	N(6)-C(17)-C(18)	112.7(4)
C(6)-C(7)-C(8)	126.5(5)	C(17)-C(18)-C(19)	124.9(7)
C(1)-N(1)-C(6)	127.2(4)	C(12)-N(6)-C(17)	126.4(4)
C(5)-N(1)-C(6)	125.4(3)	C(13)-N(6)-C(17)	125.4(4)
N(2)-C(9)-C(10)	111.8(4)	N(7)-C(20)-C(21)	112.9(4)
C(9)-C(10)-C(11)	125.4(8)	C(20)-C(21)-C(22)	123.3(6)
C(1)-N(2)-C(9)	125.9(4)	C(12)-N(7)-C(20)	126.7(4)
C(2)-N(2)-C(9)	126.4(4)	C(16)-N(7)-C(20)	125.8(3)
C(1)-H(1)---Br(2)	156.8(5)	C(12)-H(12)---Br(1)	145.8(5)
O(1)-H(1B)---N(3)	147.1(5)	C(21)-H(21)---O(1)	133.5(5)
N(5)-H(5A)---N(4)	178.2(5)	N(5)-H(5B)---O(2)	153.9(5)

3.6 Reaction of bis-(trimethylsilyl)adenine with 4-bromo-1-butene

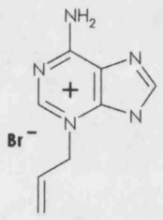
A THF solution of **3** and an excess of 4-bromo-1-butene was refluxed for 72 h, after which a yellow oil was observed to have formed. After removal of the volatiles, a thick yellow paste remained, purified by column chromatography on silica. Recrystallisation from DCM/Hexane yielded the product 3-butenyladeninium bromide **10** as very poorly soluble, air stable, faint yellow crystals (mp 165 °C), in low yield (4 %), partly as a result of the recovery procedure for the crystals. The low yield would suggest that **10** was a minor product, but thin layer chromatography suggested only the starting materials and one product were worked in the reaction, so it has to be assumed that **10** is the only product and it is produced in a low yield.



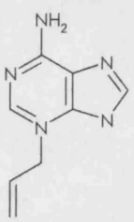
Substitution at the 3-position, rather than at either of the protected sites or the 7-position as in **9**, was unexpected, as the relative basicity of the endocyclic sites (N9 >> N7 > N3)[7] suggests that addition should typically take place at the nitrogen atoms on the five membered ring. Examples of such regiochemistry are known, however, both as organic molecules and metal complexes.[17, 18] In particular, 3-methyladenine was formed by reaction of adenine with methyl-*para*toluenesulfonate in dimethylformamide by Jones,[19] 3-allyladeninium hydrobromide was formed as part of a selection of 3-organosubstituted adenines by Abshire, by direct reaction with allyl bromide in dimethylformamide,[20] and 3-allyladenine was synthesised as a minor product in the formation of 9-allyladenine by solid-liquid phase transfer catalysis by Platzer, using potassium hydroxide and Aliquat 336 as reagents,[4] and by direct reaction with allyl bromide in dimethylformamide followed by basification by Fujii.[21]



3-methyladenine



3-allyladeninium hydrobromide



3-allyladenine

The ^{1}H NMR spectrum of **10**, in DMSO, displays multiplets at δ = 3.40 and 2.65 ppm, assigned to the methylene protons α and β to the heterocyclic nitrogen respectively. A multiplet at δ = 4.95 ppm was assigned to the terminal alkene protons, and a multiplet at δ = 5.75 ppm was assigned to the vinyl proton. In the case of the methylene protons on the butenyl moiety, the β-methylene peak is shifted further downfield than in **6**, while the α-methylene peak is further upfield. The vinyl proton peak position compares well with that of **6**, though the peak corresponding to the terminal alkenyl protons in **10** is shifted slightly downfield. Both peaks are shifted downfield relative to their corresponding peaks in the spectra of **8** [δ = 5.22 and 5.88 ppm] and **9** [δ = 5.21 and 5.88 ppm].

The $^{13}C\{^{1}H\}$ NMR spectrum of **10**, in DMSO, displays resonances at δ = 36.5 and 42.6 ppm, assigned to the carbons β and α to the nitrogen respectively. Resonances at δ = 119.4 and 132.9 ppm were assigned to the vinyl carbon and the terminal alkene carbon on the butenyl moiety respectively, and resonances at δ = 144.9, 147.3, 153.8 and 157.6 ppm were assigned to four of the five heterocyclic carbons. As in **9**, the resonance corresponding to the fifth carbon at around δ = 118.5 ppm may be obscured by the resonance corresponding to the vinyl carbon in the alkenyl moiety. Once again, the peaks corresponding to the methylene carbons in the butenyl moiety are shifted relative to the peaks observed in **6**, the β-carbon peak being further downfield and the α-carbon peak further upfield. However, the peak positions in **10** do compare well with the corresponding values in the spectra of **9** [δ = 119.3, 119.9 and 130.7, 131.6 ppm].

3.7 Structure of 4-butenyladeninium bromide (10)

Faint yellow, needle-like crystals of **10** were grown from a saturated solution of **10** in a mixture of DCM and hexane (98:2). The molecular structure of **10** is illustrated in **Figs.3.4-6**. Selected bond lengths and angles are presented in **Tables 3.11** and **3.12**. Crystallographic data is presented in **Appendix 8.8**.

The asymmetric unit of the crystal is formed of a single molecule of **9**, interacting with the bromide counterion *via* two hydrogen bonds. The butenyl group has added to the heterocyclic ring in the 3-position [N(3)-C(31) 1.470(3) Å], with the butenyl moiety perpendicular to the plane of the molecule (**Fig 3.5**). The N-C_{α} bond length [N(3)-C(31) 1.470(3) Å] compares well with its counterpart in 9-butenyladenine [1.472 Å][22] and **8** [1.373(5)-486(6) Å]. The C=C bond length [C(33)-C(34) 1.301(6) Å] is considerably longer than in 9-butenyladenine [1.238 Å],[22] though compares more favourably with three of the four of those in **9** [1.263(10)-1.289(8) Å]. The butenyl moiety has caused a slight distortion in the

six-membered ring in order to accommodate it, lengthening the C(3)-N(3) distance [1.374(3) Å] relative to that of thymine [1.349(3) Å].[23]

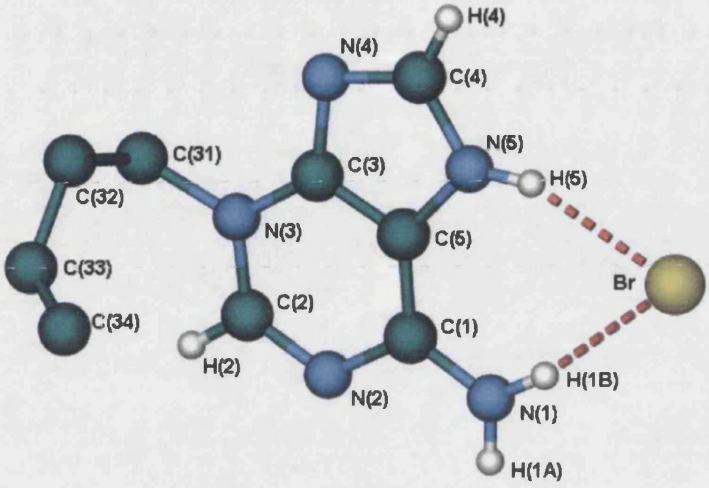


Fig.3.4 The asymmetric unit of 10

The presence of the butenyl moiety on the nitrogen in the 4-position has caused the six-membered ring to distort to accommodate it [C(2)-N(3)-C(3) 116.2(2)°] compared to 9-butenyladeinine [C(2)-N(3)-C(3) 109.6°].[22] and adenine [C(2)-N(3)-C(3) 109.6°].[23] The first part of the butenyl moiety [N(3)-C(31)-C(32) 111.0(2)°, C(31)-C(32)-C(33) 111.0(2)°] has marginally wider bond angles than those in 9-butenyladenine [N-C_α-C_β 112.0°, C_α-C_β-C_γ 114.2°],[22] but the angle between the C=C bond and rest of the butenyl moiety [C(32)-C(33)-C(34) 125.1(3)°] is more acute than in 9-butenyladenine [C_β-C_γ-C_δ 129.4°].[22] This may be due in part to the packing arrangement in **10** (**Fig.3.5**) where sheets of adenine molecules are separated by a layer of butenyl moieties. The C=C termini of the moieties may be subject to steric repulsion as they are brought into close proximity with each other.

The molecule forms polymeric sheets, held together alternately by a network of hydrogen bonds centred around two bromide ions, and two C-H---N hydrogen bonds [C(2)-H(2)---N(4) 2.362(2) Å, C(31)-H(31B)---N(2) 2.500(2) Å], [C(2)-H(2)---N(4) 170.6(5)°, C(31)-H(31B)---N(2) 142.7(5)°]. The C-H---N bonds are unexpected, but compare well in length to similar examples of C-H---N bonds such as in methylpyrazine [2.44(2)-2.76(2) Å][24] and **4** (2.446(5) Å). **10** interacts strongly with the bromide counterion, forming multiple interactions *via* a C-H---Br bond [C(4)-H(4)---Br 2.877(2) Å, 175.4(5)°] from the five-

membered ring, an N-H---Br bond [N(5)-H(5)---Br 2.405(2) Å, 159.4(5)°], and two N-H---N bonds [N(1)-H(1A)---Br 2.652(2) Å, 162.4(5)°] [N(1)-H(1B)---Br 2.586(2) Å, 167.9(5)°].

Table 3.11: Selected bond lengths (Å) for 3-butenyladeninium bromide (10)

N(3)-C(31)	1.470(3)	C(1)-N(1)	1.315(3)
C(31)-C(32)	1.527(4)	N(1)-H(1A)	0.880(2)
C(32)-C(33)	1.493(5)	N(1)-H(1B)	0.880(2)
C(33)-C(34)	1.301(6)	N(5)-H(5)	0.880(2)
H(2)---N(4)	2.362(2)	H(31B)---N(2)	2.500(2)
H(1A)---Br	2.652(2)	H(1B)---Br	2.586(2)
H(4)---Br	2.877(2)	H(5)---Br	2.405(2)

Table 3.12: Selected bond angles (°) for 3-butenyladeninium bromide (10)

N(3)-C(31)-C(32)	111.0(2)	C(2)-N(3)-C(31)	122.0 (2)
C(31)-C(32)-C(33)	111.0(2)	C(3)-N(3)-C(31)	121.8 (2)
C(32)-C(33)-C(34)	125.1(3)	C(2)-N(3)-C(3)	116.2(2)
C(2)-H(2)---N(4)	170.6(5)	C(31)-H(31B)---N(2)	142.7(5)
N(1)-H(1A)---Br	162.4(5)	N(1)-H(1B)---Br	167.9(5)
C(4)-H(4)---Br	175.7(5)	N(5)-H(5)---Br	159.4(5)

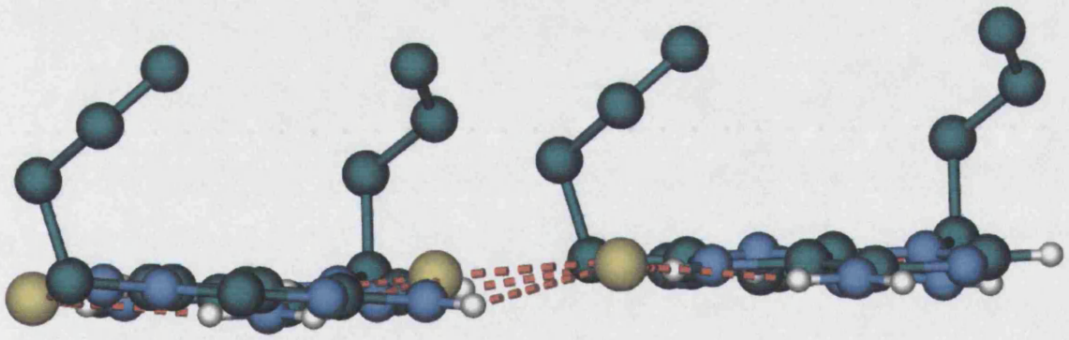


Fig.3.5 Perpendicularity of butenyl moiety to the plane of the molecule

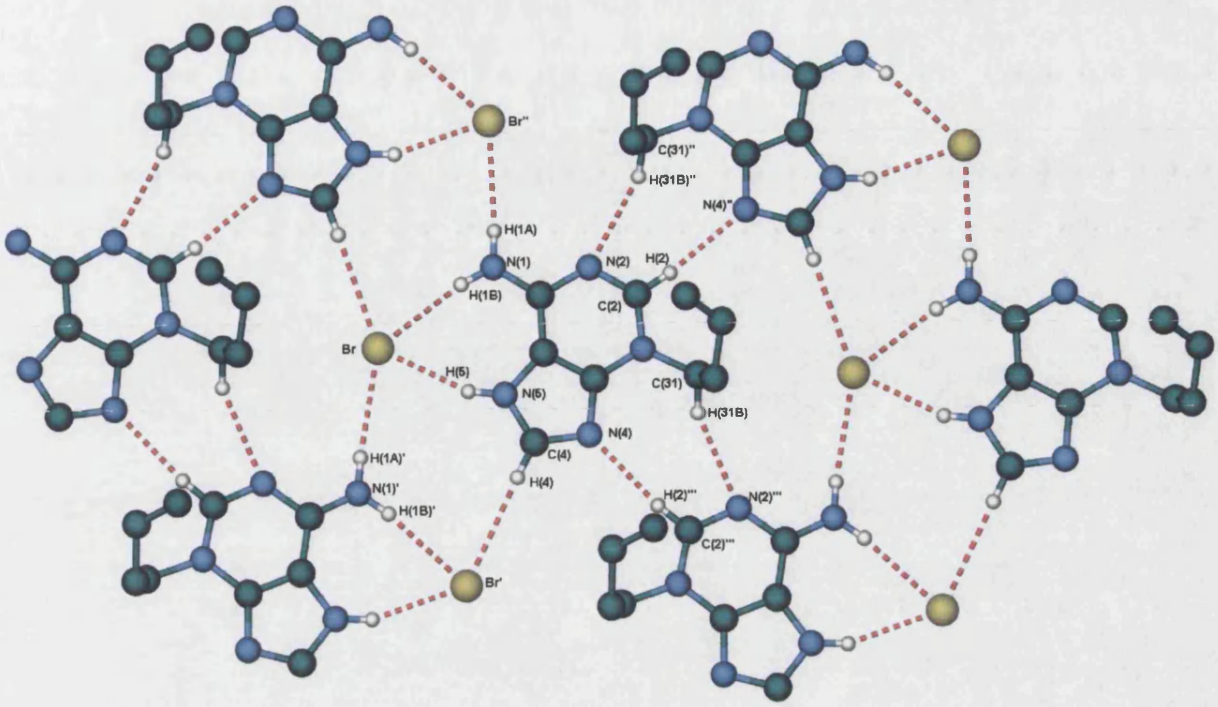
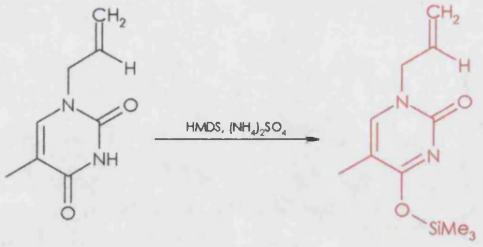


Fig.3.6 Extended structure of 10

3.8 Synthesis of (trimethylsilyl)-1-allylthymine

A mixture of HMDS, 1-allylthymine (**5**) and a few crystals of ammonium sulphate was refluxed for 18 h. After removal of the volatiles, a colourless oily liquid remained, identified as the product (trimethylsilyl)-1-allylthymine **11** (93%).



The driving force behind the reaction is the formation of a strong Si-O bond, which occurs at the least sterically hindered of the carbonyl groups, in the 4-position, *para* to the allyl moiety. Despite the same stoichiometry between HMDS and DNA base as in the formation of **1**, no peaks were observed in the NMR corresponding to a silyl group protecting the 2-position, suggesting in this case that steric factors influence the regiochemistry of the

silylation. The allyl group effectively blocks the carbonyl group in the 2-position, directing the reaction to protect only the 4-position.

The ^{1}H NMR spectrum of **11** displays a doublet (J = 1.0 Hz) at δ = 1.92 ppm, assigned to the methyl protons on the ring. A doublet (J = 6.0 HZ) at δ = 4.27 ppm was assigned to the methylene protons on the allyl moiety, and multiplets at δ = 5.27 and 5.90 ppm to the terminal alkenyl and vinyl proton respectively. A doublet (J = 1.1 Hz) at δ = 6.98 ppm was assigned to the carbon-bonded ring proton. The observed peak positions mostly correspond very well to those of **5**, as would be expected, though the peak corresponding to the heterocyclic proton in **11** was shifted very slightly upfield upon resilylation compared to **5** [δ = 7.08 ppm].

The $^{13}C\{^{1}H\}$ NMR spectrum of **11** displays a resonance at δ = 12.5 ppm, assigned to the carbon of the methyl group on the heterocyclic ring. A resonance at δ = 51.5 ppm was assigned to the methylene carbon on the allyl moiety, and resonances at δ = 118.9 and 132.6 ppm were assigned to the vinyl and terminal alkenyl carbons, respectively. Resonances at δ = 106.1, 143.9, 156.5 and 170.3 ppm were assigned to the heterocyclic carbons. The peaks corresponding to the methyl carbon, and the vinyl and terminal alkenyl protons on the allyl moiety compare well with those of **5**, though the peak corresponding to the methylene carbon is shifted slightly downfield upon resilylation [δ = 49.8 ppm].

3.9 Structure of (trimethylsilyl)-1-allylthymine (11)

Thin, needle-like crystals of **11** spontaneously formed from a saturated solution of **11** in HMDS. The molecular structure of **11** is illustrated in **Figs.3.7** and **3.8**. Selected bond lengths and angles are presented in **Tables 3.13** and **3.14**. Crystal structure data is presented in **Appendix 8.9**.

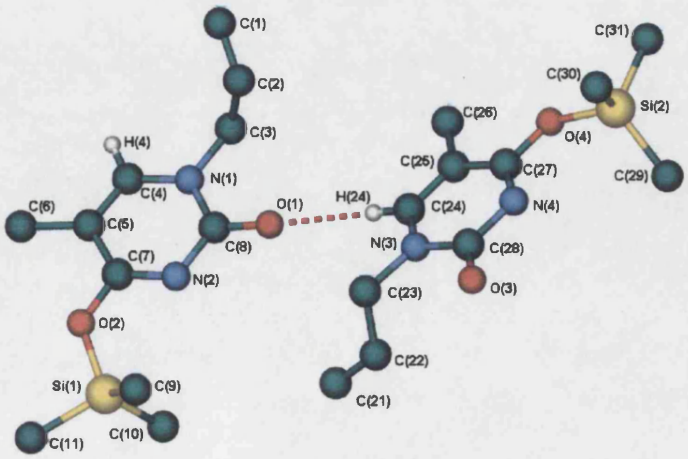


Fig.3.7 Structure of the asymmetric unit of 11

The asymmetric unit is formed of two molecules of **11**, held together by a C-H---O hydrogen bond. The silyl group has protected the less sterically hindered of the carbonyl groups [Si(1)-O(2) 1.6982(13) Å, O(4)-Si(2) 1.6866(15) Å], with the silicon atom in the plane of the molecule. The Si-O bond length compares well to the complementary group in **1** [1.6951(16) Å], though is once again long in comparison to similar bonds in other compounds, such as in *hexa*-(trimethylsiloxy)benzene [Si-O 1.655(3) Å, 1.673(4) Å].[25] The heterocyclic ring is moderately distorted [C(7)-N(2) 1.304(5) Å C(7)-C(5) 1.418(5) Å] due to the steric bulk of the $SiMe_3$ group relative to that of thymine [C(7)-N(2) 1.401(5) Å, C(7)-C(5) 1.453(4) Å].[26]

The bulk of the $SiMe_3$ group has caused the C-O-Si bond to widen from the tetrahedral [C(7)-O(2)-Si(1) 126.31(12)°, C(27)-O(4)-Si(2) 126.79(13)°] in order to accommodate it, to a greater extent than in bis(trimethylsilyl)thymine (**1**) [C-O-Si 125.46(14)°].

The molecule forms a polymeric chain (**Fig.3.8**) interacting via C-H---O hydrogen bonds [C(4)-H(4)---O(3) 2.34(5) Å, 163.9(10)°; C(24)-H(24)---O(1) 2.29(5) Å, 158.8(10)°], of comparable length with those in bis(trimethylsilyl)cytosine **2** [H(1)---O(2) 2.26(3) Å], though once again longer than similar examples of C-O---H hydrogen bonds, such as in 1-methylcytosine [H(1)---O(2) 2.04(2) Å].[15] The steric bulk of the allyl moiety has caused the molecules to alternate in their orientation relative to the axis of the chain, the moieties above and below the heterocyclic rings. This interaction contrasts with the structure of **1**, in which no intermolecular interaction is observed. The unprotected carbonyl group in **11** is free to form hydrogen bonds, and interacts with the closest hydrogen to form the observed chain structure.

Table 3.13: Selected bond lengths (Å) for (trimethylsilyl)-1-allylthymine (11)

N(1)-C(3)	1.475(2)	N(3)-C(23)	1.473(2)
C(3)-C(2)	1.502(3)	C(23)-C(22)	1.480(3)
C(2)-C(1)	1.291(3)	C(22)-C(21)	1.310(4)
C(8)-O(1)	1.237(2)	C(28)-O(3)	1.230(2)
C(7)-O(2)	1.344(2)	C(27)-O(4)	1.339(2)
O(2)-Si(1)	1.6892(13)	O(4)-Si(2)	1.6866(15)
C(5)-C(6)	1.502(3)	C(25)-C(26)	1.505(3)
H(4)---O(3)	2.34(5)	H(24)-O(1)	2.29(5)

Table 3.14: Selected bond angles (°) for (trimethylsilyl)-1-allylthymine (11)

N(1)-C(3)-C(2)	111.48(16)	N(3)-C(23)-C(22)	112.46(17)
C(3)-C(2)-C(1)	122.9(2)	C(23)-C(22)-C(21)	123.6(2)
C(4)-N(1)-C(3)	119.90(16)	C(24)-N(3)-C(23)	119.55(17)
C(8)-N(1)-C(3)	118.61(16)	C(28)-N(3)-C(23)	118.56(16)
C(4)-N(1)-C(8)	121.43(16)	C(24)-N(3)-C(28)	121.88(16)
C(7)-O(2)-Si(1)	126.31(12)	C(27)-O(4)-Si(2)	126.79(13)
N(2)-C(7)-O(2)	117.83(17)	N(4)-C(27)-O(4)	117.84(18)
C(5)-C(7)-O(2)	116.34(16)	C(25)-C(27)-O(4)	116.74(17)
C(5)-C(7)-N(2)	125.81(17)	C(25)-C(27)-N(4)	125.42(17)
C(4)-H(4)---O(3)	163.9(10)	C(24)-H(24)---O(1)	158.8(10)

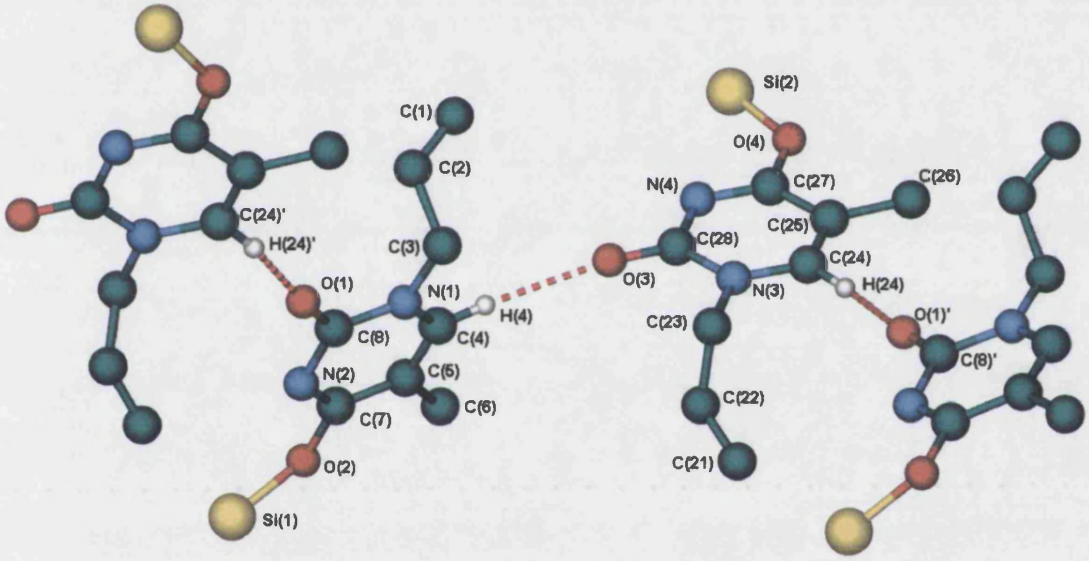
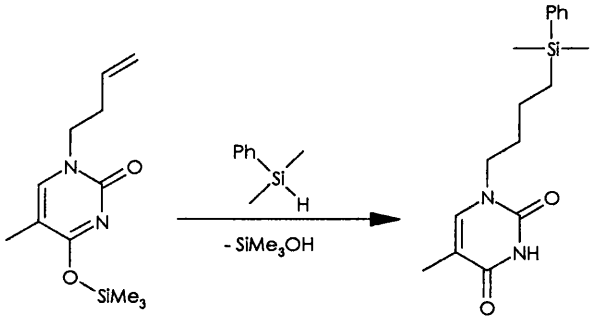


Fig.3.8 Chain structure of 11. Symmetry operator 3/2-x, y-1/2, ½+z

3.10 Hydrosilylation of 1-butenylthymine with phenyldimethylsilane

With a high yield of trimethylsilyl-1-allylthymine (**11**) from 1-allylthymine (**5**), it was of great interest to attempt a further step and to attempt a hydrosilylation of a protected alkenylthymine using a simple silane. 1-butenylthymine (**6**) was selected as the alkenylthymine for this purpose, as it is producible in still acceptable yields and the greater separation between the olefin and the DNA base than in **5** may serve to improve the regioselectivity of the reaction.

A mixture of 1-butenylthymine (**6**), hexamethyldisilazane and a few crystals of ammonium sulphate were refluxed for 18 h, after which the opacity due to solid **6** had cleared. After removal of the volatiles, a thick, colourless oil remained that was not isolated, presumed to be (trimethylsilyl)-1-butenylthymine. To this was added dimethylformamide, phenyldimethylsilane and a catalytic amount of chloroplatinic acid in propan-2-ol, and the mixture was heated at 110 °C until the liquid IR spectrum revealed an absence of starting material by a lack of peak at 2160 cm^{-1} corresponding to a Si-H stretching frequency. After removal of the volatiles, an oily grey solid remained, purified by column chromatography, using a mixture of dichloromethane and methanol as eluent. Recrystallisation from a hexane/dichloromethane mixture yielded the product (4-phenyldimethylsilyl)butylthymine (**12**) as colourless crystals (51 %, mp 130-2 °C).



12

The phenyldimethylsilane has added across the sterically unhindered double bond, rather than to the endocyclic double bond. Only the ω-silyl isomer has been recovered, suggesting that the steric bulk of the phenyl group has directed the hydrosilylation to add silicon at the terminal end of the olefin and form a "linear" product.

The ^1H NMR spectrum of **12** displays multiplets at δ = 0.78, 1.33 and 1.68 ppm, assigned to the methylene protons α, β and γ to the silicon respectively. These peak positions increasingly contrast with those of 4-(phenyldimethylsilyl)-1-bromobutane (**13**) [δ = 0.74, 1.45, 1.82 ppm], discussed in the next chapter, displaying a change in the environment of the methylene groups from being bonded exclusively to bromide to being bonded to the thymine group. The electronegativity of nitrogen is marginally higher than that of bromine (N 3.04, Br 2.96),[27] and it may be that the interaction between the α-methylene protons and the nitrogen in the 1-position in thymine is more polar than between the same protons and bromide, pushing the peak due to those protons further downfield. **12** displays a sharp singlet at δ = 1.91 ppm which was assigned to the protons on the exocyclic methyl group, and a triplet (J = 7.0 Hz) at δ = 3.67 ppm, assigned to the methylene protons α to the nitrogen, comparing well with those

of 1-butenylcytosine (**6**). It also displays multiplets at δ = 7.32 and 7.49 ppm, assigned to the protons in the phenyl group, and a broad singlet at δ = 8.92 ppm, assigned to the heterocyclic amine proton. This peak occurs considerably further upfield than in the spectra of 1-alkenylthymines (N-H δ = 9.84-10.65), and suggests a less polarized N-H bond in **12** than in its precursor.

The $^{13}C\{^{1}H\}$ NMR spectrum of **12** displays peaks at δ = 12.3, 21.0, 32.7 and 47.9 ppm, assigned to the methylene protons α, β, γ and δ to the silicon respectively. It also displays a peak at δ = 15.40 ppm, assigned to the exocyclic methyl carbon, and peaks at δ = 110.4, 140.4, 150.9 and 164.3 ppm, assigned to the four carbons in the heterocyclic ring.

The ^{29}Si NMR spectrum of **12** displays a single peak at δ = -3.0, the same as the corresponding peaks in the ^{29}Si NMR spectra of 4-(phenyldimethylsilyl)-1-bromobutane and 2-phenyl-2,6-disilaheptane.[28]

3.11 Structure of (4-phenyldimethylsilyl)butylthymine (12)

Colourless, tabular crystals of **12** were grown from a saturated solution of **12** in dichloromethane with trace amounts of hexane. The molecular structure of **12** is illustrated in **Figs.3.9** and **3.10**. Selected bond lengths and angles are presented in **Tables 3.15** and **3.16**. Crystal structure data is presented in **Appendix 8.10**.

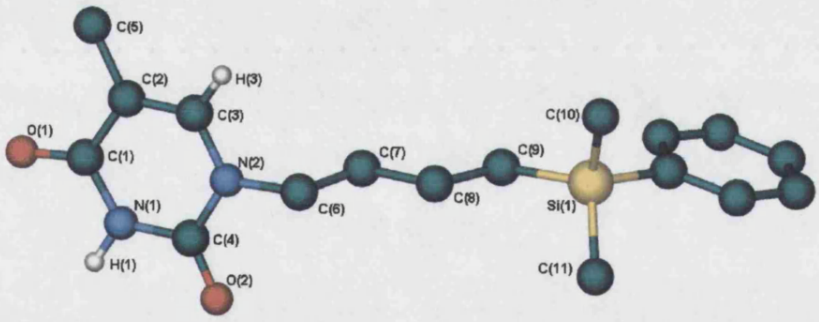


Fig.3.9 Asymmetric unit of 12

The asymmetric unit of the crystal is formed of a single molecule of **12**. The hydrosilylation has taken place at the exocyclic olefin to form a C-Si single bond [C(9)-Si(1) 1.8771(18) Å]. There appears to be no distortion of the bond distances in the heterocyclic ring [C(4)-N(1) 1.3861(19) Å, C(1)-N(1) 1.381(2) Å, C(1)-C(2) 1.445(2) Å] relative to thymine [C(4)-N(1) 1.361(4) Å, C(1)-N(1) 1.401(5) Å, C(1)-C(2) 1.453(4) Å],[26] and the N-CH_2 bond distance [N(2)-C(6) 1.4777(19) Å] compares well to the relative distance in **10** [1.475(6) Å],

11 [1.475(2) Å, 1.473(2) Å] and 9-allyladeninium chloride hydrate [1.474 Å].[14] The C-Si bond distance in the alkyl moiety [C(9)-Si(1) 1.8771(18) Å] is also similar to the bond length between the alkyl moiety and the dimethylphenyl silicon in 4-hydroxy-1-(1-hydroxy-2-propyl)-6-methylene-3-(2-(dimethyl(phenyl)silyl)ethyl)cyclohexene [1.865(3) Å].[29]

The alkyl moiety does not appear to have caused the heterocyclic ring to distort [C(3)-N(2)-C(4) 121.48(13)°, N(1)-C(4)-N(2) 114.62(13)°, C(1)-N(1)-C(4) 126.83(14)°] relative to the same angles in thymine [C(3)-N(2)-C(4) 122.5(3)°, N(1)-C(4)-N(2) 115.5(2)°, C(1)-N(1)-C(4) 126.3(3)°].[26] The bond angles around the alkyl moiety [C(3)-N(2)-C(4) 121.48(13)°, C(3)-N(2)-C(6) 119.59(13)°, C(4)-N(2)-C(6) 118.76(13)°] also compare very favourably to those around the allyl moiety in **11** [C(3)-N(2)-C(4) 121.43(16)°, 121.88(16)°; C(3)-N(2)-C(6) 119.90(16)°, 119.55(17)°; C(4)-N(2)-C(6) 118.61(16)°, 118.56(16)°].

The molecule forms a dimer (**Fig.3.10**) held together by two symmetry-related N-H---O hydrogen bonds [H(1)---O(1) 1.911(10) Å, 172.77(15)°]. The length of the bond is short compared to similar bonds in other compounds, such as 1-methylcytosine [H(1)---O(2) 2.04(2) Å][15] and bis-(trimethylsilyl)cytosine (**2**) [2.26(3) Å], suggesting a relatively strong interaction. Certainly, the dimerisation is not disfavoured on steric grounds, with the bulky ω-silylalkyl groups removed from each other.

Table 3.15: Selected bond lengths (Å) for (4-phenyldimethylsilyl)butylthymine (12)

N(2)-C(6)	1.4777(19)	C(1)-C(2)	1.445(2)
C(6)-C(7)	1.514(2)	C(1)-O(1)	1.2378(19)
C(7)-C(8)	1.526(2)	C(4)-O(2)	1.2199(19)
C(8)-C(9)	1.530(2)	N(2)-C(3)	1.374(2)
C(9)-Si(1)	1.8771(18)	N(2)-C(4)	1.374(2)
C(1)-N(1)	1.381(2)	N(1)-H(1)	0.88(2)
C(4)-N(1)	1.3861(19)	H(1)---O(1)	1.911(10)

Table 3.16: Selected bond angles (°) for (4-phenyldimethylsilyl)butylthymine (12)

N(2)-C(6)-C(7)	113.86(13)	N(1)-C(4)-N(2)	114.62(13)
C(6)-C(7)-C(8)	110.25(13)	N(1)-C(4)-O(2)	121.56(14)
C(7)-C(8)-C(9)	114.09(14)	N(2)-C(4)-O(2)	123.82(14)
C(8)-C(9)-Si(1)	113.66(12)	N(1)-C(1)-C(2)	115.65(13)
C(3)-N(2)-C(4)	121.48(13)	N(1)-C(1)-O(1)	120.32(14)
C(3)-N(2)-C(6)	119.59(13)	C(2)-C(1)-O(1)	124.05(14)
C(4)-N(2)-C(6)	118.76(13)	N(1)-H(1)---O(1)	172.77(15)
C(1)-N(1)-C(4)	126.83(14)		

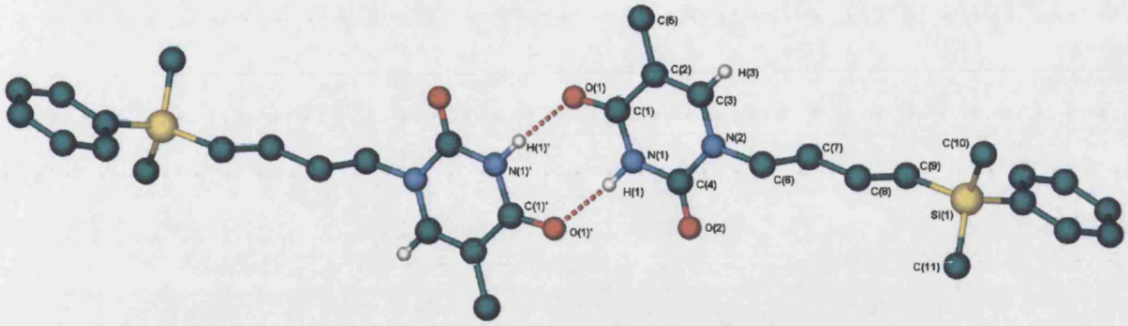


Fig.3.10 Hydrogen bonding in 12. Symmetry operator 2-x, 1-y, 1-z

3.12 Conclusions

A general method has been established for the formation of 1-alkenylthymines in high purity and acceptable yield. 1,3-bisallylcytosinium bromide (**8**) 7,9-bisallyladeninium bromide hydrate (**9**), 3-butenyladeninium bromide (**10**), (trimethylsilyl)-1-allylthymine (**11**) and (4-phenyldimethylsilyl)butylthymine (**12**) have been synthesised in very low yield but crystallographic purity, and structurally characterised by X-ray diffraction. **8** forms a dimer *via* interaction with the bromide counterion, and a ladder structure via further molecule-bromide hydrogen bonds. **9** was shown to display extensive hydrogen bonding in the solid, forming a network incorporating water of crystallisation and the bromide ion. **10** interacts with itself *via* two C-H---N hydrogen bonds and forms highly structured sheets *via* interaction with the bromide ion, **11** forms a chain structure *via* C-H---O hydrogen bonds, and **12** forms a hydrogen bonded dimer *via* two N-H---O hydrogen bonds.

Unfortunately, the results achieved suggest that while the addition of a ω-bromoolefin to a protected DNA base followed subsequent hydrosilylation can be used effectively, as in the formation of **12**, the alkylation step produces results that are too varied and in too low yield to provide a family of hydrosilylation precursors containing the other bases for further investigation. While the compounds produced involving adenine and cytosine are of structural interest, they contribute no further to attempts to link silicon and DNA bases *via* alkyl chains, and as such are of little use to the proposed synthesis of a siloxane polymer with pendant DNA bases. It follows that the second proposed method (**Scheme.3.1**), where α-silyl-ω-bromides are added to protected bases by substitution, is of more interest for the purposes of the investigation.

3.13 Experimental

3.2 Synthesis of 1-alkenylthymines

A THF (50 cm^3) solution of bis-(trimethylsilyl)thymine (**1**) and an excess of alkenyl bromide were refluxed until the IR spectrum displayed no further generation of the product, monitored by charting the growth of the peak at ca 1750 cm^{-1} due to carbonyl groups on thymine. The THF and excess alkenyl bromide were then removed under reduced pressure. Data for the amounts of reactants used is presented in **Table 3.17**.

Table 3.17: Reactant amounts and reaction times for the synthesis of 5-7

		(2)		Alkenyl Bromide		
	Akenyl Bromide	g	mmol	cm^3	mmol	**Reaction Time (h)**
5	Allyl Bromide	11.0	41	13.0	150	72
6	4-bromo-1-butene	3.0	11	3.0	30	72
7	5-bromo-1-butene	3.0	11	2.6	22	144

In the case of allyl bromide, the reaction afforded a yellow oil from which the product 1-allylthymine (**5**) spontaneously crystallised. Two recrystallisations from toluene liberated the pure product as white platelets (5.5 g, 81 %).

In the cases of 4-bromo-1-butene and 5-bromo-1-pentene, the reactions afforded brown oils that were chromatographed on silica with a mixture of dichloromethane and methanol (98:2). The chromatography yielded one band, which afforded the crude alkenylthymine. Two recrystallisations from toluene yielded the pure product. 1-butenylthymine (**6**) was recovered as white platelets (1.17g, 59 %). 1-pentenylthymine (**7**) was recovered as brown needles (0.38 g 18 %).

1-butenylthymine (**6**): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.68 (bs, 1H, N*H*), 6.98 (s, 1H, $C_{ty}H$), 5.76 (m, 1H, $C_{vinyl}H$), 5.10 (m, 2H, CH=CH_2), 3.78 (t, J = 7.0 Hz, 2H, N-CH_2), 2.47 (m, 2H, N-CH_2CH_2), 1.92 (s, 3H, CH_3); ^{13}C NMR (300 MHz, $CDCl_3$): δ = 164.6 (C_{ty}), 151.0 (C_{ty}), 140.7 (C_{ty}), 133.5 (CH=*C*H_2), 118.5 (*C*$_{vinyl}$), 110.4 (C_{ty}), 48.0 (N-*C*H_2), 33.3 (N-CH_2*C*H_2), 12.3 (C_{ty}-*C*H_3); *analysis* calcd for $C_9H_{12}N_2O_2$: C 60.0, H 6.71, N 15.6 %, found C 60.0, H 6.58, N 15.6 %.

1-pentenylthymine (**7**): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.84 (bs, 1H, N*H*), 6.98 (s, 1H, $C_{ty}H$), 5.79 (m, 1H, $C_{vinyl}H$), 5.05 (m, 2H, CH=CH_2), 3.71 (t, J = 7.3 Hz, 2H, N-CH_2), 2.11 (m, 2H, N-CH_2CH_2), 1.92 (s, 3H, CH_3), 1.80 (m, 2H, N-CH_2CH_2CH_2); ^{13}C NMR (300 MHz, $CDCl_3$): δ = 164.7 (C_{ty}), 151.2 (C_{ty}), 140.5(C_{ty}), 133.6.9 (CH=*C*H_2), 115.8 (*C*$_{vinyl}$), 110.6 (C_{ty}),

48.0 (N-CH_2), 30.4 (N-CH_2CH_2), 28.0 (m, 2H, N-$CH_2CH_2CH_2$), 12.3 (C_{ty}-CH_3); *analysis* calcd for $C_{10}H_{14}N_2O_2$: C 61.8, H 7.27, N 14.4 %, found C 61.4, H 7.18, N 14.1 %.

3.3 Reaction of bis-(trimethylsilyl) DNA bases with allyl bromide

THF solutions (25 cm^3) of bis-(trimethylsilyl)cytosine (**2**) and bis-(trimethylsilyl)adenine (**3**) and an excess of allyl bromide were refluxed for 72 h. The THF and excess allyl bromide were then removed by reduced pressure. Data for the amounts of reactants used is presented in **Table 3.18.**

Table 3.18: Reactant amounts for the synthesis of 8,9

		Silylated Base		Allyl Bromide	
	Protected Base	g	mmol	cm^3	mmol
8	Cytosine	0.22	1.96	0.63	7.2
9	Adenine	5.0	37	11.9	132

In each case, the reactions afforded thick immiscible oils. In the case of bis-(trimethylsilyl)cytosine, the oil was recrystallised once from chloroform to yield the product 1,3-bisallylcytosinium bromide **8** as sparingly soluble, air stable, white crystals (0.11 g, 9 %). In the case of bis-(trimethyladenine), the oil was recrystallised three times from chloroform to yield the product 1,3-bisallyladeninium bromide **9** as very sparingly soluble, air stable, orange crystals (0.44 g 4 %).

1,3-bisallylcytosinium bromide (**8**): ^{1}H NMR (300 MHz, DMSO): δ = 7.98 (d, J = 8.0 Hz, s, 1H, C_{cy}-*H*), 6.20 (d, J = 8.0 Hz, s, 1H, C_{cy}-*H*), 5.88 (m, 1H, C_{vinyl}*H*), 5.22 (m, 2H, CH=CH_2), 4.60 (d, J = 5.0 Hz, 2H, N-CH_2), 4.46 (d, J = 5.0 Hz, 2H, N-CH_2); ^{13}C NMR (75 MHz, DMSO): δ = 158.6 (C_{cy}), 147.7 (C_{cy}), 147.1 (C_{cy}), 131.7 (CH=*C*H_2), 129.2 (CH=*C*H_2), 118.2 (*C*$_{vinyl}$), 117.0 (*C*$_{vinyl}$), 94.1 (C_{cy}), 51.6 (N-*C*H_2), 45.3 (N-*C*H_2); *analysis* calcd for $C_{10}H_{14}N_3OBr$: C 44.1, H 5.19, N 15.4 %, found C 41.1, H 4.60, N 15.9 %.

7,9-bisallyladeninium bromide hydrate (**9**): ^{1}H NMR (300 MHz, DMSO): δ = 5.88 (m, 1H, C_{vinyl}*H*), 5.21 (m, 2H, CH=CH_2); ^{13}C NMR (75 MHz, DMSO): δ = 155.5 (C_{ad}), 151.5 (C_{ad}), 148.4 (C_{ad}), 140.0 (C_{ad}), 131.6 (CH=*C*H_2), 130.7 (CH=*C*H_2), 119.9 (*C*$_{vinyl}$), 119.3 (*C*$_{vinyl}$); *analysis* calcd for $C_{11}H_{14}N_5Br$: C 44.6, H 4.76, N 23.7 %, found C 44.4, H 4.84, N 23.9 %.

3.6 Reaction of bis-(trimethylsilyl)adenine with 4-bromo-1-butene

A THF solution (40 cm^3) of bis-(trimethylsilyl)adenine (**3**) (1.77 g, 6.34 mmol) and an excess of 4-bromo-1-butene (2.24 cm^3, 22 mmol) was refluxed for 72 h. The THF and excess 4-bromo-1-butene were then removed under reduced pressure. The reaction afforded a thick yellow paste, that was chromatographed on silica with a mixture of dichloromethane and methanol (98:2). The chromatography yielded one band, which afforded the crude product as a thick yellow oil. Recrystallisation from a mixture of dichloromethane and hexane (98:2) yielded the product 3-butenyladeninium bromide (**10**) as very sparingly soluble, air stable, faint yellow crystals (0.07 g, 4 %).

3-butenyladeninium bromide (**10**): ^{1}H NMR (300 MHz, DMSO): δ = 5.75 (m, 1H, C_{vinyl}-*H*), 4.95 (m, 2H, CH=C*H*$_2$), 3.40 (m, 2H, N-C*H*$_2$), 2.65 (m, 2H, N-CH$_2$C*H*$_2$); ^{13}C NMR (75 MHz, DMSO): δ = 157.6 (C_{ad}), 153.8 (C_{ad}), 147.3 (C_{ad}), 144.9 (C_{ad}), 132.9 (CH=*C*H$_2$), 119.4 (*C*$_{vinyl}$), 42.6 (N-*C*H$_2$), 36.5 (N-CH$_2$*C*H$_2$); *analysis* calcd for $C_9H_{12}N_5Br$: C 40.0, H 4.48, N 25.9 %, found C 40.2, H 4.51, N 25.0 %.

3.8 Reaction of 1-allylthymine with hexamethyldisilazane

A mixture of HMDS (20 cm^3, 91 mmol), 1-allylthymine (**7**) (2 g, 12 mmol) and a few crystals of ammounium sulphate was refluxed for 18 h. After this time, the solid had dissolved and a colourless solution remained. The excess HMDS was removed under reduced pressure, affording the clear oily product TMS-1-allylthymine (**11**) (2.68 g, 93%). **11** spontaneously crystallised upon cooling under nitrogen.

(trimethylsilyl)-1-allylthymine (**11**): ^{1}H NMR (300 MHz, $CHCl_3$): δ = 6.98 (d, J = 1.1 Hz, C_{ty}-*H*), 5.9 (m, 1H, C_{vinyl}-*H*), 5.27 (m, 2H, CH=C*H*$_2$), 4.27 (d, J = 6.0 Hz, 2H, N-C*H*$_2$), 1.92 (d, J = 1.0 Hz, 3H, C_{ty}-C*H*$_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.3 (C_{ty}), 156.5 (C_{ty}), 143.9 (C_{ty}), 132.6 (CH=*C*H$_2$), 118.9 (*C*$_{vinyl}$), 106.1 (C_{ty}), 51.5 (N-*C*H$_2$), 12.5 (C_{ty}-*C*H$_3$); *analysis* calcd for $C_{11}H_{20}N_2O_2Si$: C 55.0, H 8.39, N 11.7 %, found C 55.1, H 8.29, N 11.8 %.

3.10 Hydrosilylation of 1-butenylthymine with phenyldimethylsilane

A mixture of 1-butenylthymine (**6**) (0.5 g, 2.74 mmol), and excess of hexamethyldisilazane and a few crystals of ammonium sulphate were refluxed for 18 h, after which the opacity due to solid **6** had cleared. The volatiles were removed under reduced pressure, and to the remaining colourless oil was added THF (10 cm^3), phenyldimethylsilane (0.37 g, 2.74 mmol) and a catalytic amount of chloroplatinic acid in propan-2-ol, and the solution was heated to 80 °C for 72 h, after which the neat liquid IR spectrum revealed an

absence of starting material. The volatiles were removed, affording a brown solid, which was chromatographed on silica using a mixture of dichloromethane and methanol (98:2) as eluent. The chromatography yielded two bands. The first was eluted with the solvent front and afforded phenyldimethylsilane. The second was eluted at r = 0.45 and afforded the crude product as a white powder. Recrystallisation from a mixture of chloroform and hexane yielded (4-phenyldimethylsilyl)butylthymine (**12**) as colourless tabular crystals (0.43 g, 51 %).

(4-phenyldimethylsilyl)butylthymine (**12**): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.92 (bs, 1H NH), 7.49 (m, 2H, CH_{ph}), 7.32 (m, 3H. CH_{ph}), 3.67 (t, J = 7.0 Hz, 2H, N-CH_2), 1.91 (s, 3H, CH_3), 1.68 (m, 2H, NCH_2CH_2), 1.33 (m, 2H, $SiCH_2CH_2$), 0.78 (m, 2H, $SiCH_2$); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.3 (C_{thy}), 150.9 (C_{thy}), 140.4 (C_{thy}), 110.5 (C_{thy}), 47.9 (N-CH_2), 32.7 (NCH_2CH_2), 21.0 ($SiCH_2CH_2$), 15.4 (CH_3), 12.3 ($SiCH_2$); ^{29}Si NMR (60 MHz, $CDCl_3$): δ = -3.04; *analysis* calcd for $C_{17}H_{24}N_2O_2Si$: C 64.5, H 7.64, N 8.85 %, found C 63.9, H 7.64, N 8.61 %.

3.14 References

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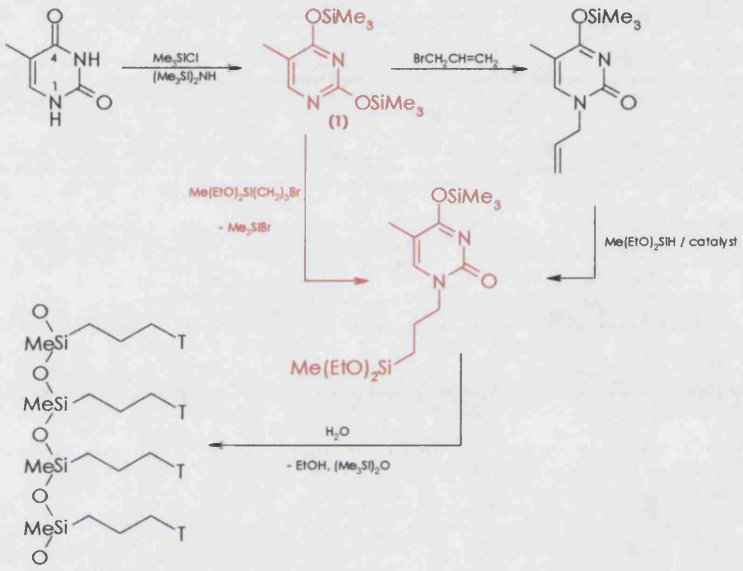
Chapter 4

Formation of ω-bromoalkylsiloxanes and addition of ω-bromoalkylsilanes to DNA Bases

4.1 Introduction

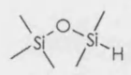
It was shown in Chapter 3 that the hydrosilylation of a protected alkenylthymine can lead to a DNA base with a pendant silylalkyl group. However, inconsistent results in the alkenylbromide substitution step caused a lack of acceptable precursors for a hydrosilylation reaction to be pursued. It follows that a study into the formation of a range of ω-silylalkyl DNA bases is not possible by this method, and pushes the investigation towards the other proposed method in the synthesis of achieving the target molecule (**Scheme 4.1**).



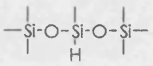
Scheme 4.1

Using this method, a silylalkyl bromide is directly substituted at a silylated DNA base, such as bis-(trimethylsilyl)thymine (**1**), ideally producing by-products that are physically different from the target molecule and can be easily removed in the work up. The compound (4-bromobutyl)dimethylphenylsilane is known, and was produced as the sole product in its synthesis, but has only been partially characterized.[1] This compound would be useful in investigating the substitution of silylalkylbromides to silylated DNA bases, so it is of interest to first optimize the hydrosilylation of 4-bromo-1-butene using phenyldimethylsilane for yield and purity. In the case of a substitution reaction involving a simple silylalkylbromide such as (4-bromobutyl)dimethylphenylsilane and a silylated DNA base, harsher conditions can be used than in the hydrosilylation of the alkenylbase with a triorganosilane, in which the catalyst would be poisoned. The use of a silyl deprotection agent such as tetrabutylammonium fluoride may aid the substitution reaction to a higher yield.

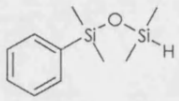
In order to more closely model a polymer with DNA bases pendant to a siloxane chain, it was of interest to form a range of siloxane systems containing pendant alkylbromide chains. Pentamethyldisiloxane (PMDS), phenyltetramethyldisiloxane (PhTMDS), and 1,1,1,3,5,5,5-heptamethyltrisiloxane (HMTS) are commercially available, and could form suitable model compounds *via* hydrosilylation of an alkenylbromide. The compound 1,3-bis(4-bromobutyl)tetramethyldisiloxane is also known,[2] but has not been prepared by the hydrosilylation of an alkenyl bromide, so it was of further interest to carry out a reaction between 4-bromo-1-butene and chlorodimethylsilane.



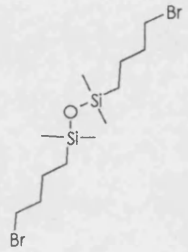
Pentamethyldisiloxane (PMDS)



1,1,1,3,5,5,5-heptamethyltrisiloxane (HMTS)



Phenyltetramethyldisiloxane (PhTMDS)

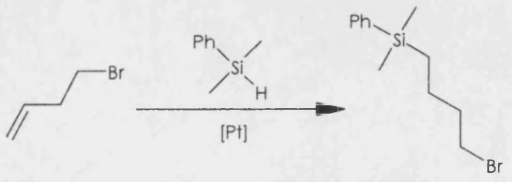


1,3-bis(4-bromobutyl)tetramethyldisiloxane

This chapter describes the synthesis of a range of silicon containing alkyl bromides, the synthesis of (4-phenyldimethylsilyl)butylthymine (**12**) *via* a substitution reaction between bis-(trimethylsilyl)thymine (**1**) and (4-bromobutyl)dimethylphenylsilane, and an extension of the methodology to other silylated DNA bases.

4.2 Hydrosilylation of 4-bromo-1-butene with phenyldimethylsilane

A mixture of 4-bromo-1-butene, phenyldimethylsilane (PhDMS) and a catalytic amount of chloroplatinic acid in propan-2-ol was heated at 80 °C for 72 h, after which the neat-liquid IR spectrum revealed an absence of starting material, specifically a lack of a peak at 2150 cm^{-1} due to a Si-H stretching vibration. After removal of the volatiles, a translucent oily liquid remained, purified by column chromatography on silica. A colourless, air-stable liquid was recovered and found to be 4-(phenyldimethylsilyl)-1-bromobutane **13** (74%).



13

The mechanism of hydrosilylation has already been discussed in the Introduction to this thesis and will not be repeated here, but it is of interest to note that formation of phenyldimethylsilane appears to be highly regioselective, the product formed being the pure terminal isomer **13**, with negligible amounts of the potential branched isomer (3-phenyldimethylsilyl)-1-bromobutane produced.

The ^{1}H NMR spectrum of **13** displays a singlet with doublet satellites (J = 7.0 Hz) at δ = 0.27 ppm, assigned to the methyl protons bonded to silicon, with proton coupling to spin active silicon with a ^{2}J(Si-H) value comparing well to other known values (6.6-7.2 Hz).[5] It also displays multiplet resonances at δ = 0.74 and 1.45 ppm, assigned to the methylene protons α and β to the silicon respectively, an apparent pentuplet (J = 6.9 Hz, overlapping triplet of triplets) at δ = 1.84 ppm, assigned to the methylene protons γ to the silicon, and a triplet (J = 6.9 Hz) at δ = 3.35 ppm, assigned to the bromomethyl protons. A multiplet at δ = 7.42 ppm was assigned to the phenyl protons. These compare well to the literature.[1]

The $^{13}C\{^{1}H\}$ NMR spectrum of **13** displays a resonance at δ = -3.1 ppm, corresponding to the methyl carbons attached to silicon, comparing well with the corresponding peak in the spectrum of 2-phenyl-2,6-disilaheptane [Ph-Si(CH_3)$_2$ δ = -3.0][6]. It displays resonances at δ = 14.8, 22.5, 33.4 and 36.2 ppm, assigned to the carbons α, β, γ and δ to the silicon, respectively. The α, β and γ peaks compare favourably with corresponding peaks in the spectrum of the analogous (4-chlorobutyl)phenyldimethylsilane [δ = 15.1, 21.3, 36.2].[7] Resonances at δ = 127.8, 128.9, 129.2, 133.0, 133.5 and 139.1 ppm were assigned to the aromatic carbons.

The ^{29}Si NMR spectrum of **13** displays a single resonance at δ = -3.0, further downfield than peaks corresponding to silicon in similar compounds, such as 2-phenyl-2,6-disilaheptane [Ph-*Si* δ = -4.1].[6] Phenyldimethylsilane displays a ^{29}Si NMR resonance at δ = -16.9,[8] confirming that the silicon environment had been significantly altered as a result of the reaction.

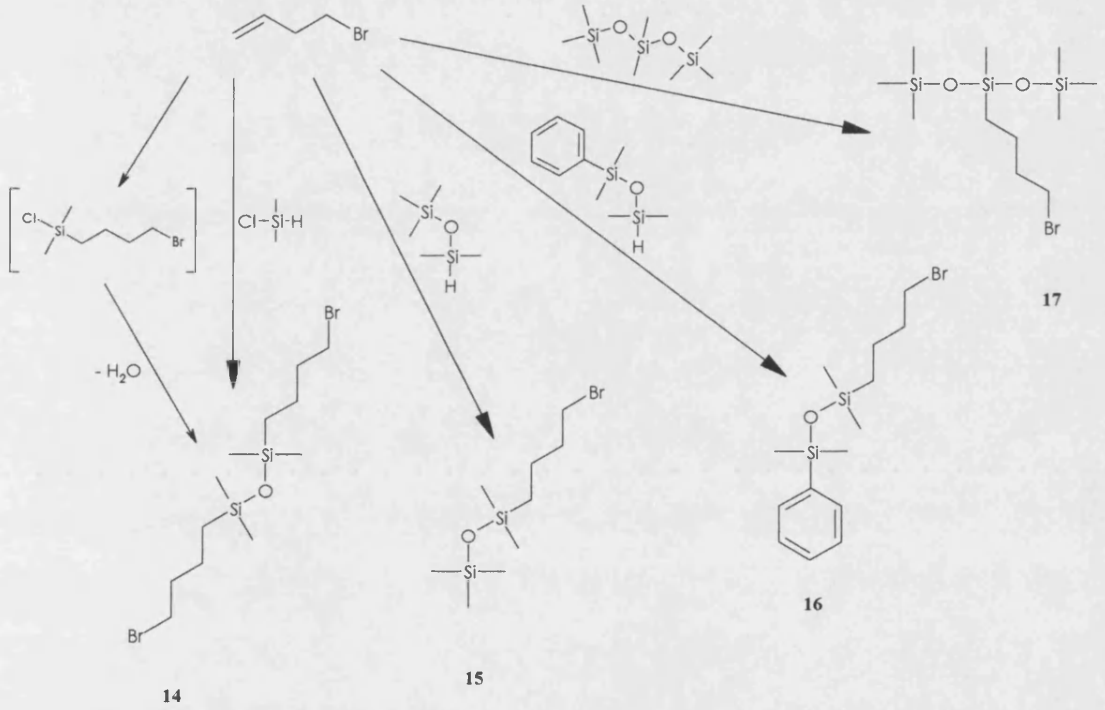
4.3 Hydrosilylation of 4-bromo-1-butene to form (4-bromobutyl)alkylsiloxanes

A mixture of 4-bromo-1-butene, the siloxane in question and a catalytic amount of chloroplatinic acid in propan-2-ol was heated at 110 °C until the neat-liquid IR spectrum revealed an absence of starting material, denoted by an absence of Si-H stretching peak at 2150 cm^{-1}. After removal of the volatiles, translucent grey liquids remained, purified by

column chromatography on silica with chloroform as the eluent. In each case, the 4-bromobutylsiloxane product (**15-17**) was afforded with the solvent front as an air-stable, colourless oil.

4.3a Hydrosilylation of 4-bromo-1-butene with chlorodimethylsilane

A mixture of 4-bromo-1-butene, chlorodimethylsilane and a catalytic amount of chloroplatinic acid in propan-2-ol was heated at 110 °C until the neat-liquid IR spectrum revealed an absence of starting material, again denoted by lack of Si-H stretching vibration at 2150cm^{-1}. The volatiles were removed and the remaining grey liquid was hydrolysed, washed with water, extracted with chloroform and dried over $MgSO_4$. Column chromatography on silica with chloroform as eluent afforded the 1,3-bis-(4-bromobutyl)siloxane product (**14**) as an air stable, colourless oil.



Pertinent reaction and physical data for the reactions is presented in **Table 4.1**.

Table 4.1: Reaction data for synthesis of 4-bromobutylsiloxanes

	Siloxane	Reaction Time (h)	Yield (%)
14	TMDS	72	79
15	PMDS	72	61
16	PhTMDS	72	56
17	HMTS	96	79

In each case, thin layer chromatography revealed only one reaction product, and only the terminal bromobutylsiloxane was recovered, suggesting that negligible amounts of branched side products were formed in the reaction.

The ^{1}H and $^{13}C\{^{1}H\}$ spectra of the four compounds were comparable with each other, and are presented in **Tables 4.2** and **4.3**.

Table 4.2: Selected ^{1}H NMR data (ppm) for 4-bromobutylsiloxanes

	14	**15**	**16**	**17**
Si-C*H*$_3$	0.07	0.06 0.07	0.05 0.33	-0.09 -0.08
Si-C*H*$_2$-CH$_2$- (m, 2H)	0.52	0.52	0.52	0.37
Si-CH$_2$-C*H*$_2$- (m, 2H)	1.48	1.45	1.45	1.38
-C*H*$_2$-CH$_2$Br (m, 2H)	1.88	1.83	1.83	1.77
-CH$_2$-C*H*$_2$Br (t, J = 7.0 Hz 2H)	3.42	3.35	3.35	3.31

Table 4.3: Selected $^{13}C\{^{1}H\}$ NMR data (ppm) for 4-bromobutylsiloxanes

	14	**15**	**16**	**17**
Si-*C*H$_3$	0.7	0.6 0.7	0.4 0.6	-2.4 -2.2
Si-*C*H$_2$-CH$_2$-	17.0	16.5	16.5	14.6
Si-CH$_2$-*C*H$_2$-	21.6	21.1	21.0	19.9
-*C*H$_2$-CH$_2$Br	33.3	32.8	32.6	31.6
-CH$_2$-*C*H$_2$Br	35.7	35.3	35.2	34.1

There is a general trend in both types of spectrum where resonances assigned to protons and carbon atoms in **14** appear slightly further downfield than in **15** and **16**, and in turn those in **15** and **16** appear slightly further downfield than in **17**. In **14**, the two chemically equivalent bromoalkyl groups may cause the Si-O-Si linkage to become slightly more polarised, an effect lessened where there is only one bromoalkyl group in **15**. In **17**, greater chemical stability may be provided by a longer siloxane chain, providing a slightly less polarised environment for the bromoalkyl group. This may be borne out by the trend in the ratio of methylene groups in the alkyl chain to oxygen atoms in the siloxane fragment, and therefore in the relative amounts of alkyl chain and siloxane in the molecule. In the case of **14**, the methylene:oxygen ratio is 4:1, in **15** and **16** it is 4:2, and in **17** it is 4:3. This increasing

siloxane component may chemically stabilise the alkyl chain, pushing the peaks due to the methylene carbons further upfield.

The ^{29}Si NMR data of the four compounds are presented in **Table 4.4**.

Table 4.4: ^{29}Si NMR Data For 4-bromobutylsiloxanes

	^{29}Si NMR (δ, ppm)
14	7.0 (O-*Si*Me_2-CH_2)
15	7.0 (O-*Si*Me_2-CH_2), 7.6 (Me_3*Si*-O)
16	7.3 (O-*Si*Me_2-CH_2), 8.6 ($PhMe_2$*Si*-O)
17	7.5 (Me_3*Si*-O), -22.5 (O_2*Si*Me-CH_2)

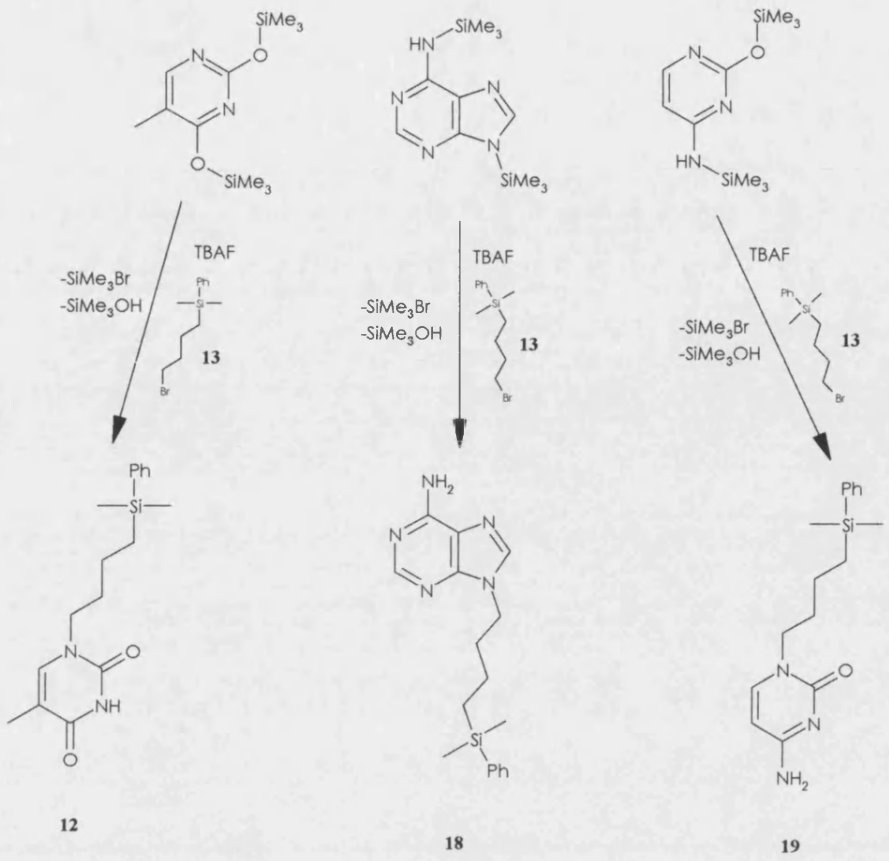
The dimethyl siloxane peak in **17** [δ = -22.5 ppm] occurs slightly further upfield than in octamethyltrisiloxane [O_2*Si*Me_2 δ = -20.8 ppm],[9] though the trimethylsiloxy peak [δ = 7.5 ppm] occurs further downfield [Me_3*Si*-O δ = 7.1 ppm],[9] as does that in **15** [δ = 7.6 ppm]. The phenyldimethylsiloxy peak position in **16** is slightly upfield from the corresponding peak in methoxydimethylsilylbenzene [$PhMe_2$*Si*-O δ = 8.4 ppm].[10]

4.4 Reaction of 4-(phenyldimethylsilyl)-1-bromobutane with silylated DNA bases

A solution of 4-(phenyldimethylsilyl)-1-bromobutane (**13**), the silylated DNA base in question and tetrabutylammonium fluoride (TBAF) was refluxed for 72 h. After removal of the volatiles, grey or brown solids remained, which were purified by chromatography on silica followed by recrystallisation of the target compound, yielded in each case as air-stable, highly soluble crystals. Pertinent reaction and physical data are presented in **Table 4.5**.

Table 4.5: Reaction data for synthesis of (4-phenyldimethylsilyl)butyl DNA bases

	Silylated Base	Yield (%)	Crystals	Melting Point (°C)
12	Thymine	74	Colourless tablets	132-133
18	Adenine	55	White needles	124-126
19	Cytosine	45	Colourless	140-142



The crystals of **12** produced in this reaction were identical in colour and appearance to those produced by the hydrosilylation of 1-butenylthymine (**6**), and had identical NMR spectra and melting point. The yield of **12,** however, is higher in the case of the substitution of 4-(phenyldimethylsilyl)-1-bromobutane (**13**) with bis-(trimethylsilyl)thymine (**1**) (74 %) than in the hydrosilylation of **6** with phenyldimethylsilane (51 %).

13 has undergone substitution with **1** in the 1-position, as in the formation of 1-allylthymine (**5**) by substitution of allyl bromide with **1**. The NMR spectra of the reaction mixture prior to purification gave no indication of any reaction with the nitrogen in the 3-position, so it is assumed that **12** is the only product.

In contrast to the similarity between the formations of **5** and **12**, the substitution of Br in **13** using silylated adenine and cytosine appears to be more regioselective than the similar reaction with alkenyl bromides, discussed in Chapter 3. In the cases of alkenyl bromide substitution with bis-(trimethylsilyl)adenine (**3**) and bis-(trimethylsilyl)cytosine (**2**), multiple allyl groups can be attached to the base and form salts. 4-bromo-1-butene also reacts with **3** in the 3-position, again forming a salt. As a result of the substitution of **13** with **2** and **3**, however, both **18** and **19** contain only one silylalkyl moiety, in the 9-position in the case of

18, and the 1-position in the case of **19**. The most basic nitrogen atom in adenine is that in the 9-position,[11] so the regiochemistry in the formation of **18** is as expected. Other substitutions of adenine have taken place preferentially at the 9-position, such as the formation of 9-methyladenine by reaction of free adenine with methyliodide in the presence of sodium hydride,[12] and 9-allyladenine formed from the reaction of free adenine with allyl bromide in the presence of base,[13] a different method to that used to form 7,9-bisallyladeninium bromide in this investigation, where allyl bromide was reacted with bis-(trimethylsilyl)adenine (**3**) in DMF.

In all three (4-phenyldimethylsilyl)butyl-DNA base-forming reactions, the substitution has taken place exclusively at a protected site on the DNA base and only once, forming a neutral compound. In each case, the addition of the silylalkyl group has significantly increased the solubility of the base in polar solvents such as chloroform, in the same way that the addition of a bromoolefin to thymine caused a similar increase. The silylalkylation reaction appears to cause a considerable change in the solubility properties of the base, and suggests that similarly modified bases pendant to siloxane or polysiloxane structures may exhibit a similar increase in solubility.

The ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of the silylalkyl moieties on **18** and **19** are similar to each other, and are presented in **Tables 4.6** and **4.7**, along with those of **13** and **12**, discussed previously, for comparison.

Table 4.6: Selected ^{1}H NMR data (ppm) for (4-phenyldimethylsilyl)butyl DNA bases

	13	**12**	**18**	**19**
Si-C*H*$_3$	0.27	0.27	0.25	0.26
Si-C*H*$_2$-CH$_2$- (m, 2H)	0.74	0.78	0.80	0.76
Si-CH$_2$-C*H*$_2$- (m, 2H)	1.84	1.33	1.37	1.35
-C*H*$_2$-CH$_2$N$_{Base}$ (m, 2H)	1.45	1.68	1.89	1.59
-CH$_2$-C*H*$_2$N$_{Base}$ (t, 2H)	3.35[a]	3.63	4.15	3.60

[a] *CH$_2$Br*

Table 4.7: Selected $^{13}C\{^1H\}$ NMR data (ppm) for (4-phenyldimethylsilyl)butyl DNA bases

	13	12	18	19
Si-CH_3	-3.1	-3.1	-3.2	-3.1
Si-CH_2-CH_2-	14.8	12.3	15.2	15.4
Si-CH_2-CH_2-	22.5	21.0	21.0	21.0
-CH_2-CH_2 N_{Base}	33.4	32.7	33.6	32.7
-CH_2-CH_2 N_{Base}	36.2[a]	47.9	43.4	49.9

[a] CH_2Br

Additionally, the ^1H NMR spectrum of **18** shows a broad peak at δ = 5.65 ppm, assigned to the protons on the primary amine, and at δ = 7.69 and 8.36 ppm, assigned to the protons bonded directly to the heterocyclic ring. These values are consistent with those observed in the NMR spectra of bis-(trimethylsilyl)adenine (**3**).

The ^1H NMR spectrum of **19** shows peaks at δ = 5.86 and 7.13 ppm, assigned to the two protons bonded directly to the ring, and a peak at δ = 8.02 ppm, assigned to the primary amine protons.

The ^{29}Si NMR spectra of **18** and **19** were also similar, and data are presented in **Table 4.8** along with those of **13** and **12** for comparison.

Table 4.8: ^{29}Si NMR data (ppm) for (4-phenyldimethylsilyl)butyl DNA bases

	^{29}Si NMR (δ)
13	-3.0
12	-3.0
18	-3.1
19	-3.1

The similarity of the ^{29}Si NMR spectra with each other is expected, as the silicon atoms in the four compounds are in very chemically similar environments.

4.5 Structure of (4-phenyldimethylsilyl)butylcytosine (19)

Colourless, tabular crystals of **19** were grown from a saturated solution of **19** in a hexane/dichloromethane mixture. The molecular structure of **19** is illustrated in **Figs.4.1** and **4.2**. Selected bond lengths and angles are presented in **Tables 4.9** and **4.10**. Crystallographic data is presented in **Appendix 8.11**.

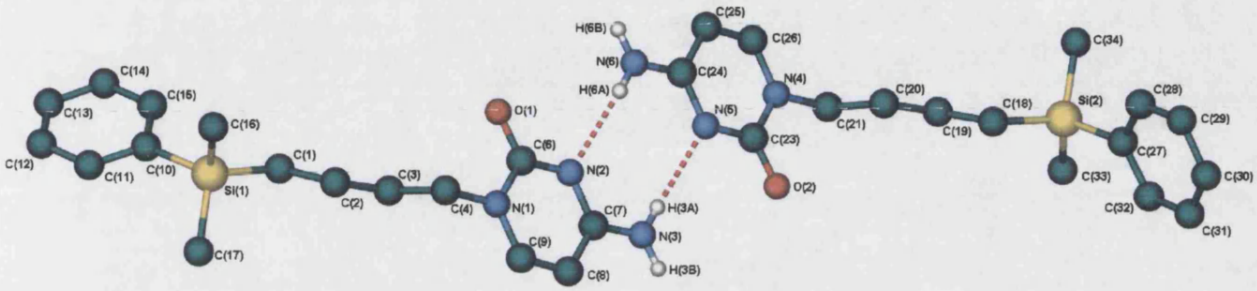


Fig.4.1 Asymmetric unit of 19. symmetry operator 2-x, -y, -z-2

The asymmetric unit of the crystal is formed of two independent molecules of **19**. The substitution has taken place at the nitrogen in the 1-position, to form an N-alkyl moiety [N(1)-C(4) 1.477(3) Å, N(4)-C(21) 1.476(3) Å], with an N-C bond comparing well to that of (4-phenyldimethylsilyl)butylthymine (**12**) [1.4777(19) Å], (trimethylsilyl)-1-allylthymine (**11**) [1.475(2) Å, 1.473(2) Å] and 9-allyladeninium chloride hydrate [1.474 Å].[14] The bond lengths in the alkyl moiety compare well with those of **12** [C_α-C_β 1.514(2) Å, C_β-C_γ 1.526(2) Å, C_γ-C_δ 1.530(2) Å], though the C-Si bond distance in **19** [C(18)-Si(2) 1.869(2) Å] is longer than the analagous bond in **12** [C_δ-Si 1.8771(18) Å].

The bond angles around the N^1 position [C(6)-N(1)-C(9) 119.97(14)°, C(6)-N(1)-C(4)119.51(14)°, C(9)-N(1)-C(4) 120.49(14)°, C(23)-N(4)-C(26) 120.45(14)°, C(23)-N(4)-C(21) 119.69(13)°, C(26)-N(4)-C(21) 119.84(14)°] are very close to 120°, less distorted than those in **12** (C(3)-N(2)-C(4) 121.48(13)°, C(3)-N(2)-C(6) 119.59(13)°, C(4)-N(2)-C(6) 118.76(13)°). The bond angles in the alkyl moiety itself are also different to those in the alkyl moiety in **12** (C_α-C_β-C_γ 110.25(13)°, C_β-C_γ-C_δ 114.09(14)°, C_γ-C_δ-Si 113.66(12)°). In comparison, the C_α-C_β-C_γ angle in **19** is more obtuse [C(4)-C(3)-C(2) 111.95(12)°, C(21)-C(20)-C(19) 112.71(12)°], the C_β-C_γ-C_δ angle is more acute [C(3)-C(2)-C(1) 113.15(12)°, C(20)-C(19)-C(18) 112.63(12)°], and the C_γ-C_δ-Si angle is considerably more obtuse [C(2)-C(1)-Si(1) 115.37(12)°, C(19)-C(18)-Si(2) 116.68(12)°]. The chain has straightened at its

termini and bent increasingly in the middle. This may be as a result of the extended hydrogen bonding present in **19**, discussed below, which is not present in **12**.

The molecule forms a dimer held together by two N-H---N hydrogen bonds [H(6A)---N(2) 2.193(10) Å, 154.10(12)°], [H(3A)---N(5) 2.202(10) Å, 151.74(12)°], considerably shorter than those in bis-(trimethylsilyl)adenine (**3**) (2.38(1) Å), but of comparable length with those in bis-(trimethylsilyl)cytosine (**2**) (2.26(3) Å, 2.24(3) Å) and 1-methylcytosine (2.14(2) Å).[15] It also forms a laddered structure of dimers *via* two symmetry-related N-H---O hydrogen bonds [H(6B)---O(1) 2.012(12) Å, 161.13(11)°]. These are longer than those in **12** (1.911(10) Å), but shorter than those in **2** (2.26(3) Å). They are of comparable length with those in 1-methylcytosine [H(1)---O(1) 2.04(2) Å],[15] suggesting a similar strength intermolecular interaction.

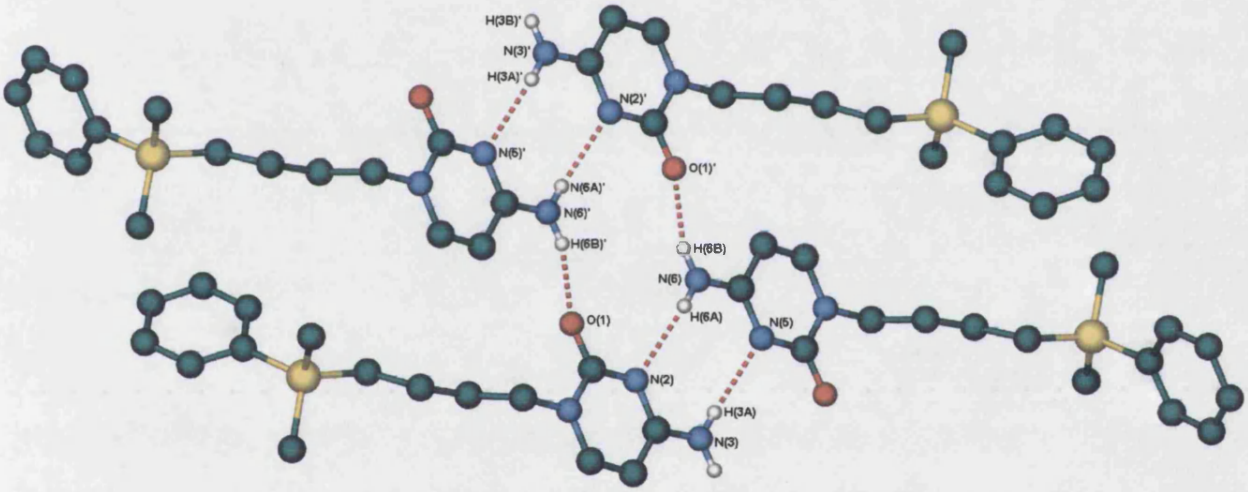


Fig.4.2 Hydrogen bonding pattern in 19.

Table 4.9: Selected bond lengths (Å) for (4-phenyldimethylsilyl)butylcytosine (19)

Molecule 1		Molecule 2	
N(1)-C(4)	1.477(3)	N(4)-C(21)	1.476(3)
C(4)-C(3)	1.523(2)	C(21)-C(20)	1.519(2)
C(3)-C(2)	1.531(2)	C(20)-C(19)	1.530(2)
C(2)-C(1)	1.529(2)	C(19)-C(18)	1.527(2)
C(1)-Si(1)	1.882(3)	C(18)-Si(2)	1.869(3)
C(7)-N(3)	1.337(2)	C(24)-N(6)	1.331(2)
C(7)-N(2)	1.332(2)	C(24)-N(5)	1.339(2)
C(7)-C(8)	1.427(2)	C(24)-C(25)	1.433(2)
C(6)-O(1)	1.241(3)	C(23)-O(2)	1.239(3)
C(8)-C(9)	1.347(2)	C(25)-C(26)	1.340(2)
H(6A)---N(2)	2.193(10)	H(3A)---N(5)	2.202(10)
H(6B)---O(1)	2.012(12)		

Table 4.10: Selected bond angles (°) for (4-phenyldimethylsilyl)butylcytosine (19)

Molecule 1		Molecule 2	
N(1)-C(4)-C(3)	112.39(11)	N(4)-C(21)-C(20)	111.58(11)
C(4)-C(3)-C(2)	111.95(12)	C(21)-C(20)-C(19)	112.71(12)
C(3)-C(2)-C(1)	113.15(12)	C(20)-C(19)-C(18)	112.63(12)
C(2)-C(1)-Si(1)	115.37(12)	C(19)-C(18)-Si(2)	116.68(12)
C(6)-N(1)-C(9)	119.97(14)	C(23)-N(4)-C(26)	120.45(14)
C(6)-N(1)-C(4)	119.51(14)	C(23)-N(4)-C(21)	119.69(13)
C(9)-N(1)-C(4)	120.49(14)	C(26)-N(4)-C(21)	119.84(14)
N(3)-C(7)-C(8)	122.02(13)	N(6)-C(24)-C(25)	121.23(14)
N(2)-C(7)-N(3)	117.89(10)	N(5)-C(24)-N(6)	118.21(11)
C(8)-C(7)-N(2)	120.09(10)	C(25)-C(24)-N(5)	120.56(10)
C(6)-N(2)-C(7)	119.87(11)	C(23)-N(5)-C(24)	120.23(10)
N(6)-H(6A)---N(2)	154.10(12)	N(3)-H(3A)---N(5)	151.74(12)
N(6)-H(6B)---O(2)	161.13(11)		

4.6 Conclusions

The compounds (4-bromobutyl)phenyldimethylsilane (**13**) and 1,3-bis(4-bromobutyl)tetramethyldisiloxane (**14**) have been synthesised by the hydrosilylation of 4-bromo-1-butene with a triorganosilane, and characterised by NMR. A method has been established for the formation of α-siloxy-ω-bromoalkanes in high yield and purity. The compounds 4-bromobutylpentamethyldisiloxane (**15**), 1-(4-bromobutyl)-3-phenyltetramethyldisiloxane (**16**) and 3-(4-bromo)butylheptamethyltrisiloxane (**17**) have

been synthesised, and characterised by NMR. These bromobutylsiloxanes have been used in subsequent investigations to model more closely a siloxane polymer with pendant DNA bases. However, these siloxyalkylbromides could not use silyl deprotection reagents such as tetrabutylammonium fluoride in a substitution reaction with a protected DNA base, as the higher strength of the Si-F bond relative to the Si-O bond (Si-F 543 $kJmol^{-1}$,[3] Si-O 466 $kJmol^{-1}$)[4] would mean the fluoride would attack the siloxane linkage, forming Si-F bonds and breaking up the chain. A milder reaction would be necessary to add them to a DNA base, and will be discussed in later chapters.

13 has been substituted with silylated DNA bases to produce a new range of compounds containing a triorganosilane connected to a DNA base *via* an alkyl chain. The compounds (4-phenyldimethylsilyl)butylthymine (**12**), (4-phenyldimethylsilyl)butyladenine (**18**) and (4-phenyldimethylsilyl)butylcytosine (**19**) have been synthesised in high yield and crystalline purity, and in the case of **12**, in higher yield than by the hydrosilylation of 1-butenylthymine (**6**) with phenyldimethylsilane. Crystals of **19** have been studied by X-ray diffraction, and in the solid state was found to form a dimer *via* two symmetry N-H---N hydrogen bonds, and an extended ladder structure *via* N-H---O hydrogen bonds. While these molecules represent the final step of this branch of the investigation, they are of interest in the area of structural chemistry, and provide valuable information on the potential physical properties of a range of compounds containing siloxane fragments as opposed to simple silanes, and furthermore siloxane polymers containing pendant DNA bases.

4.7 Experimental

4.2 Hydrosilylation of 4-bromo-1-butene with phenyldimethylsilane

A mixture of phenyldimethylsilane (4.3 cm^3, 18.3 mmol), 4-bromo-1-butene (2.0 cm^3, 19.89 mmol) and a catalytic amount of chloroplatininc acid in propan-2-ol was heated to 80 °C for 72 h, after which IR spectroscopy revealed a lack of starting material by an absence of a peak at 2150 cm^{-1} corresponding to an Si-H stretching vibration. The excess 4-bromo-1-butene was removed under reduced pressure, and the remaining solution was chromatographed using chloroform as eluent. The chromatography yielded one band, eluting with the solvent front and affording the product (4-bromobutyl)phenyldimethylsilane **13** (3.7 g, 74 %). Variations on the experiment were made by varying the time of reaction between 18 h and 96 h. No improvements to the yield were made. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.42 (m, 5H, C_6H_5), 3.35 (t, J = 6.9 Hz, 2H, CH_2Br), 1.84 (m, 2H, CH_2CH_2Br), 1.45 (m, 2H, $SiCH_2CH_2$), 0.74 (m, 2H, $SiCH_2$), 0.27 (s, 6H, $Si(CH_3)_2$); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 139.1 (C_{Ph}), 133.5 (C_{Ph}), 133.0 (C_{Ph}), 129.2 (C_{Ph}), 128.9 (C_{Ph}), 127.8 (C_{Ph}), 36.2 (CH_2Br), 33.4

(CH_2CH_2Br), 22.5 ($SiCH_2CH_2$), 14.8 ($SiCH_2$), -3.1 ($Si(CH_3)_2$); ^{29}Si NMR (60 MHz, $CDCl_3$): δ = -3.0; *analysis* calcd for $C_{12}H_{19}BrSi$: C 55.1, H 7.06 %, found C 55.7, H 6.91 %.

4.3 Hydrosilylation of 4-bromo-1-butene to form (4-bromobutyl)alkylsiloxanes

A mixture of 4-bromo-1-butene, the siloxane in question and a catalytic amount of chloroplatinic acid in propan-2-ol was heated at 110 °C until the neat-liquid IR spectrum revealed an absence of starting material, denoted by an absence of Si-H stretching peak at 2150 cm^{-1}. After removal of the volatiles, translucent grey liquids remained, purified by column chromatography on silica with chloroform as the eluent. In each case, the 4-bromobutylsiloxane product was afforded with the solvent front as an air stable colourless oil.

4.3a Hydrosilylation of 4-bromo-1-butene with chlorodimethylsilane

A mixture of 4-bromo-1-butene, chlorodimethylsilane and a catalytic amount of chloroplatinic acid in propan-2-ol was heated at 110 °C until the neat-liquid IR spectrum revealed an absence of starting material, again denoted by lack of Si-H stretching vibration at 2150cm^{-1}. The volatiles were removed and the remaining grey liquid was hydrolysed, washed with water, extracted with chloroform and dried over $MgSO_4$. Column chromatography on silica with chloroform as eluent afforded the 1,3-bis-(4-bromobutyl)siloxane product as an air stable, colourless oil, recovered with the solvent front.

Reaction amounts and yields for reactions **4.3** and **4.3a** are presented in **Table 4.11**.

Table 4.11: Reactant amounts and reaction times for the synthesis of ω-bromoalkylsiloxanes

	4-bromo-1-butene Amount		Siloxane Amount		Yield	
Siloxane	cm^3	mmol	g	mmol	g	%
TMDS	4.0	39.8	3.4	36.3	5.8	79
PMDS	2.0	19.9	2.4	16.0	2.8	61
PhTMDS	2.0	19.9	3.7	16.0	3.1	56
HMTS	1.4	15.5	3.0	13.5	3.8	79

4-bromobutylpentamethyldisiloxane (**15**): ^1H NMR (300 MHz, $CDCl_3$): δ = 3.35 (t, J = 7.0 Hz, 2H, CH_2Br), 1.83 (m, 2H, CH_2CH_2Br), 1.45 (m, 2H, $SiCH_2CH_2$), 0.52 (m, 2H, $SiCH_2$), 0.07 (s, 6H, $Si(CH_3)_2$), 0.06 (s, 9H, $Si(CH_3)_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 35.3 (CH_2Br),

32.8 (CH_2CH_2Br), 21.1 ($SiCH_2CH_2$), 16.5 ($SiCH_2$), 0.7 ($Si(CH_3)_2$), 0.6 ($Si(CH_3)_3$); ^{29}Si NMR (60 MHz, $CDCl_3$): 7.6 (Me_3Si-O), 7.0 (O-$SiMe_2$-CH_2); analysis calcd for $C_9H_{23}Si_2OBr$: C 38.2, H 8.18 %, found C 38.0, H 8.01 %.

1-(4-bromobutyl)-3-phenyltetramethyldisiloxane (**16**): ^1H NMR (300 MHz, $CDCl_3$): δ = 7.45 (m, 5H, C_6H_5), 3.35 (t, J = 6.9 Hz, 2H, CH_2Br), 1.83 (m, 2H, CH_2CH_2Br), 1.45 (m, 2H, $SiCH_2CH_2$), 0.52 (m, 2H, $SiCH_2$), 0.33 (s, 6H, $Si(CH_3)_2$), 0.05 (s, 6H, $Si(CH_3)_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 139.0 (C_{Ph}), 132.2 (C_{Ph}), 132.1 (C_{Ph}), 128.5 (C_{Ph}), 128.4 (C_{Ph}), 127.0 (C_{Ph}), 35.2 (CH_2Br), 32.6 (CH_2CH_2Br), 21.0 ($SiCH_2CH_2$), 16.5 ($SiCH_2$), 0.6 ($Si(CH_3)_2$), 0.4 ($PhSi(CH_3)_2$); ^{29}Si NMR (60 MHz, $CDCl_3$): 8.6 ($PhMe_2Si$-O), 7.3 (O-$SiMe_2$-CH_2); analysis calcd for $C_{14}H_{25}Si_2OBr$: C 48.7, H 7.30 %, found C 49.0, H 7.30 %.

3-(4-bromo)butylheptamethyltrisiloxane (**17**): ^1H NMR (300 MHz, $CDCl_3$): δ = 3.31 (t, J = 7.0 Hz, 2H, CH_2Br), 1.77 (m, 2H, CH_2CH_2Br), 1.38 (m, 2H, $SiCH_2CH_2$), 0.38 (m, 2H, $SiCH_2$), -0.08 (s, 18H, $Si(CH_3)_3$), -0.09 (s, 3H, $O_2Si(CH_3)$-CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 34.1 (CH_2Br), 31.6 (CH_2CH_2Br), 19.9 ($SiCH_2CH_2$), 14.6 ($SiCH_2$), -2.2 ($O_2Si(CH_3)$-CH_2), -2.4 ($Si(CH_3)_3$); ^{29}Si NMR (60 MHz, $CDCl_3$): 7.5 (Me_3Si-O), -22.5 (O_2SiMe-CH_2); analysis calcd for $C_{11}H_{29}Si_3O_2Br$: C 37.0, H 8.18 %, found C 37.4, H 8.18 %.

4.4 Reaction of 4-(phenyldimethylsilyl)-1-bromobutane with silylated DNA bases

A solution of 4-(phenyldimethylsilyl)-1-bromobutane (**13**) (50 cm^3), the silylated DNA base in question and tetrabutylammonium fluoride (TBAF) was refluxed for 72 h. Reaction amounts and yields are presented in **Table 4.12**.

Table 4.12: Reactant amounts and reaction times for the synthesis of ω-silylalkyl DNA bases

			ω-silylalkylbromide		Silylbase		TBAF		Yield	
	DNA Base	Solvent	g	mmol	g	mmol	g	mmol	g	%
12	Thymine	THF	1.0	3.69	1.0	3.69	0.96	3.69	0.86	74
18	Adenine	Xylene	0.55	2.03	0.56	2.02	0.53	2.04	0.34	55
19	Cytosine	Xylene	1.22	4.50	1.15	4.50	1.19	4.55	0.61	45

After removal of the volatiles, grey or brown solids remained, purified by chromatography on silica, using a mixture of dichloromethane and methanol as eluent (98:2). In each case, the chromatography yielded three bands. The first eluted with the solvent front and was found to be unreacted **13**. The second band eluted at approximately r = 0.7 and was found to be TBAF. The third eluted at between r = 0.75 and 0.45 and was found to be the target product. The products were washed with water to extract any further traces of remaining TBAF, and were recrystallised from a mixture of dichloromethane and hexane, yielding the pure product as colourless, tabular crystals in the cases of **12** and **19** and as extremely fine white needles in the case of **18**.

(4-phenyldimethylsilyl)butyladenine (**18**): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.36 (s, 1H, C_{ad}-*H*), 7.69 (s, 1H, C_{ad}-*H*), 5.65 (bs, 2H, NH_2), 4.15 (t, J = 7.0 Hz, 2H, N-CH_2), 1.89 (m, 2H, NCH_2CH_2), 1.37 (m, 2H, $SiCH_2CH_2$), 0.80 (m, 2H, $SiCH_2$), 0.25 (s, 6H, $Si(CH_3)_2$); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 43.4 (N-CH_2), 33.6 (NCH_2CH_2), 21.0 ($SiCH_2CH_2$), 15.2 ($SiCH_2$) -3.2 ($Si(CH_3)_2$); ^{29}Si NMR (60 MHz, $CDCl_3$): δ = -3.1; *analysis* calcd for $C_{17}H_{23}N_5Si$: C 62.7, H 7.12, N 21.5 %, found C 61.9, H 7.13, N 21.3 %.

(4-phenyldimethylsilyl)butylcytosine (**19**): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.02 (bs, 2H, NH_2), 7.13 (D, J = 1.0 Hz, 1H, C_{cy}-*H*), 5.86 (D, J = 1.0 Hz, 1H, C_{cy}-*H*), 3.60 (t, J = 7.0 Hz, 2H, N-CH_2), 1.59 (m, 2H, NCH_2CH_2), 1.35 (m, 2H, $SiCH_2CH_2$), 0.76 (m, 2H, $SiCH_2$), 0.26 (s, 6H, $Si(CH_3)_2$); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 49.9 (N-CH_2), 32.7 (NCH_2CH_2), 21.0 ($SiCH_2CH_2$), 15.5 ($SiCH_2$) -3.1 ($Si(CH_3)_2$); ^{29}Si NMR (60 MHz, $CDCl_3$): δ = -3.1; *analysis* calcd for $C_{16}H_{23}N_3OSi$: C 63.8, H 7.69, N 13.9 %, found C 63.6, H 7.8, N 13.6 %.

4.8 References

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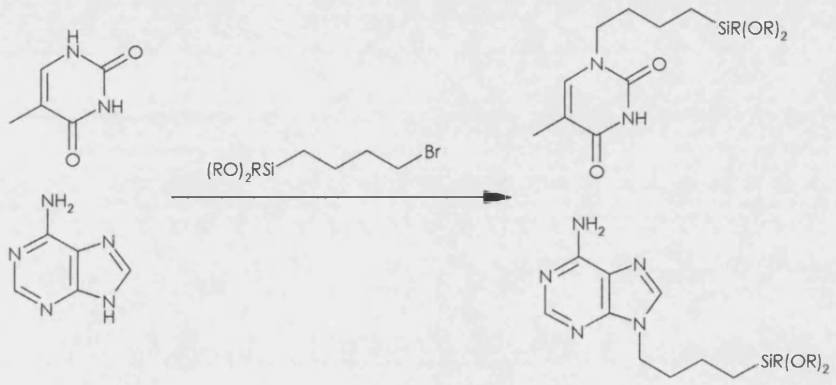
Chapter 5

Addition of ω-bromoalkylsiloxanes to DNA bases

5.1 Introduction

In order to closer model a polysiloxane chain with pendant DNA bases, it was of interest to synthesise simple oligosiloxanes with a pendant DNA base. The bromoalkylsiloxanes (Chapter 4) have been shown to be available in high yield and purity via the hydrosilylation of 4-bromo-1-butene, so it is of interest to investigate a method of directly substituting these compounds with a DNA base to produce the desired model compounds (**Scheme 5.1**).



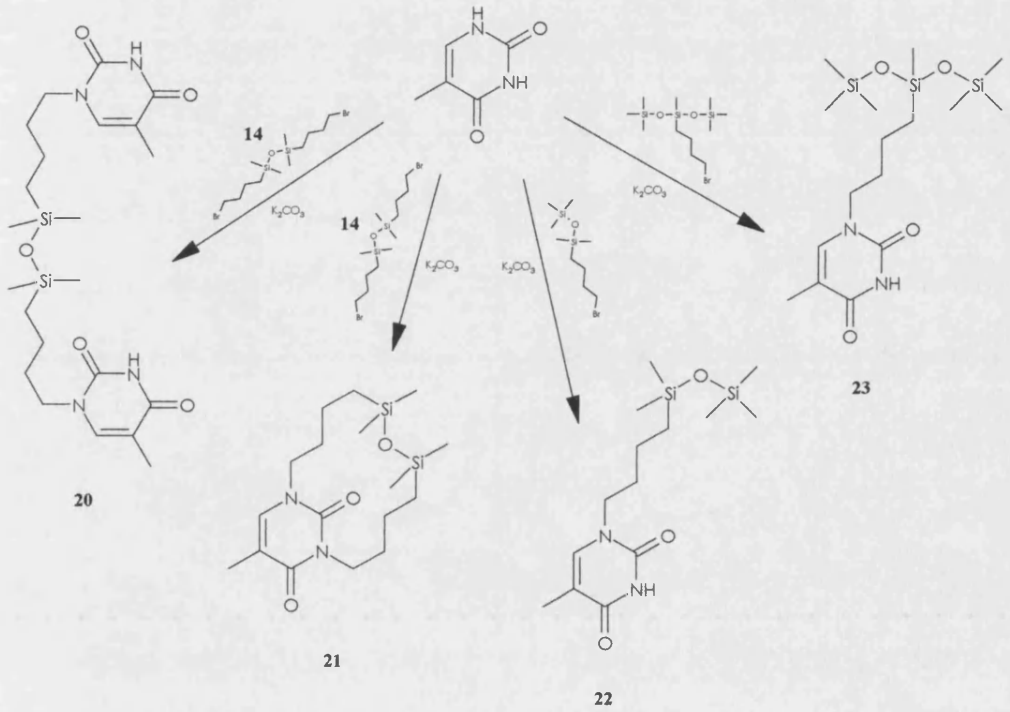
Scheme 5.1

TBAF cannot be used in the same manner as in the addition of **13** to silylated DNA bases (Chapter 4), as the higher strength of the Si-F bond relative to the Si-O bond (Si-F 543 $kJmol^{-1}$,[1] Si-O 466 $kJmol^{-1}$)[2] means the fluoride could attack the siloxane linkage, as is common in the deprotection of a silyl ether,[3, 4] forming Si-F bonds and breaking up the chain. Another reagent must be used in order to drive the reaction forward under milder conditions than previously discussed substitutions involving TBAF (Chapter 4), while still producing by-products that can be easily separated from the target compounds during the work up stage. Potassium carbonate has been shown to act well as a base in N-alkylation reactions involving alkyl bromides and purine derivatives under mild conditions in DMF, neutralising the HBr produced as a by-product of the reaction.[5] It is possible that this method could extend to similar reactions involving other DNA bases.

This chapter describes the addition of four of the bromoalkylsiloxanes described in Chapter 4 to adenine and thymine, and also the addition of 1,3-bis(4-bromobutyl)tetramethyldisiloxane to cytosine, and the characterisation of the products.

5.2 Substitution of thymine with bromoalkylsiloxanes

A DMSO solution of thymine, potassium carbonate and the appropriate bromoalkylsiloxane (**Scheme 5.2**) was stirred for 72 h, after which a voluminous white, water soluble precipitate had formed in the reaction mixture. After filtration, in the case of the addition of 1,3-bis(4-bromobutyl)tetramethyldisiloxane (**14**) to thymine, a product spontaneously crystallised in the filtrate when left to stand for 48 hours, and was found to be the neutral, air stable 14-membered ring product 6,6,8,8,15-pentamethyl-7-oxa-1,13-diaza-6,8-disila-bicyclo[11.3.1]heptadec-15-ene-14,17-dione (**21**), containing one disiloxane and one molecule of thymine.



Scheme 5.2

In all other cases, upon removal of the volatiles from the filtrate, a white powder remained which was washed repeatedly with water to remove all possible traces of DMSO. Thin layer chromatography of the remaining powder suggested a mixture of three components. The first, eluted with the solvent front, was found to be unreacted siloxane, the second was found to be traces of DMSO, and the third was the siloxyalkylthymine in low yield in each case. In each case, a white powder that did not elute remained was assumed to be the unreacted DNA base. The crude siloxyalkylthymine was recrystallised from various solvents, but no crystallographic quality samples were recovered.

Pertinent reaction data for reactions with thymine is presented in **Table 5.1**. ^{1}H and $^{13}C\{^{1}H\}$ NMR data are presented in **Tables 5.2** and **5.3** respectively. ^{29}Si NMR data for the products involving thymine, adenine and cytosine are presented at the end of the results of the three experiments in **Table 5.10** and discussed separately.

Table 5.1: Reaction data for substitution of thymine with bromoalkylsiloxanes

	Siloxane	Yield (%)	Melting Point (°C)
20	TMDS	8	135-7
21	TMDS	8	127
22	PMDS	14	118-20
23	HMTS	11	85-87

In each case, the alkyl bromide has substituted with a heterocyclic secondary amine and formed an N-alkyl product, typically favouring the more basic 1-position over the 3-position,[6] and forming water-soluble potassium bromide with the potassium carbonate in the reaction mixture. The formation of neutral, monoalkylated products is consistent with other reactions with thymine carried out in this investigation, forming 1-alkenyl- and 1-silylalkylthymines. In the case of **21**, despite the excess of thymine present in the reaction mixture, the disiloxane has reacted with the N^1 and N^3 positions of a single molecule of thymine to form a 14-membered ring, considerably more soluble in polar solvents, such as chloroform, than the monoalkylated products. All of the products were recovered in low yield, considerably lower than other examples of the reaction in which an alkyl bromide was added to a DNA base derivative using potassium carbonate as a reagent.[5] Possible reasons for these low yields may be the low solubility of the free DNA base in the reaction solvents, and losses of product incurred in the purification process. Considerable quantities of white powders that were assumed to be the unreacted DNA bases were observed during column chromatography of the products, suggesting that the reaction did not proceed to completion and the process of purification did not cause significant loss of product.

The ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of the four new compounds are similar, and are presented in **Tables 5.2** and **5.3**.

Table 5.2: ^{1}H NMR (ppm) data for siloxyalkyl thymines

	20	21	22	23
Si-CH_2-CH_2- (m, 2H)	0.54	0.52 (4H)	0.54	0.54
Si-CH_2-CH_2- (m, 2H)	1.34	1.35 (4H)	1.35	1.35
-CH_2-CH_2N_1 (m, 2H)	1.70	1.74 (4H)	1.70	1.70
-CH_2-CH_2N_1 (t, 2H)[a]	3.70 (J = 7.3 Hz) *3.96 (J = 7.4 Hz)*[a] *4.11*[b]	4.16 (m, 4H)	3.68 (J = 7.3 Hz) *3.93 (J = 7.4 Hz)*	3.68 (J = 7.3 Hz) *3.91 (J = 7.5 Hz)*
C_{ar}-*H*	6.98	6.99	7.01	6.96
C_{ar}-CH_3	1.92	1.99	1.96	1.91
N-*H*	8.57	N/A	8.64	8.62

[a]Italics: Secondary peaks corresponding to products formed by addition at N^3 position at thymine

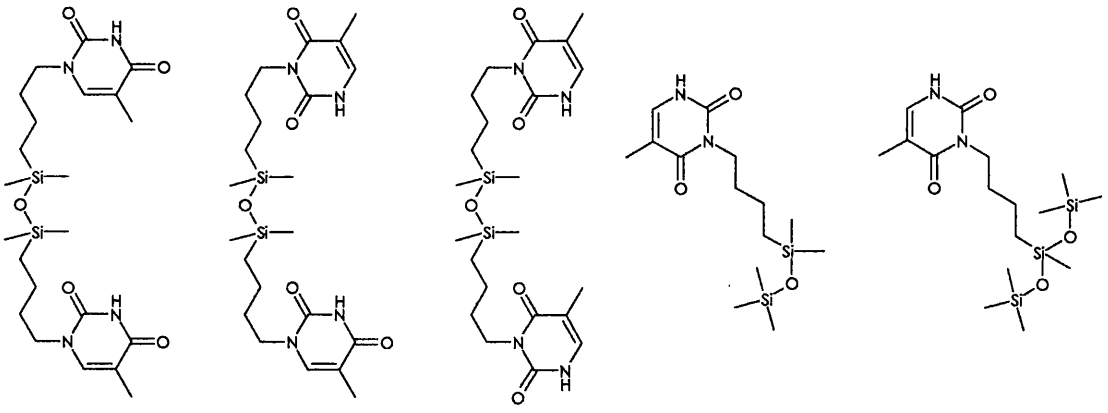
[b]Signal too weak to measure J

Table 5.3: $^{13}C\{^1H\}$ NMR (ppm) data for siloxyalkyl thymines

	20[a]	21	22[a]	23
Si-*C*H_2-CH_2-	12.5	12.5	12.5	10.5
Si-CH_2-*C*H_2-	18.9 *19.3*	18.8 19.3	18.8	18.3
-*C*H_2-CH_2N_1	30.9 *32.9*	30.9 32.9	30.9	30.5
-CH_2-*C*H_2N_1	39.99 *46.7*	39.9 46.7	39.9 *46.3*	46.5
C_{ar}-*C*H_3	17.4	17.4	15.9	15.3
C$_{ar}$	109.4	109.4	108.5	108.6
	137.2	137.2	138.4	138.6
	151.9	151.9	148.7	148.8
	163.1	163.1	162.1	162.2

[a]Italics: Secondary peaks corresponding to products formed by addition at N^3 position at thymine

There are several instances of secondary peaks in these NMR spectra corresponding to minor products formed by 3-addition to thymine instead of 1-addition (**20a, 20b, 22a, 23a**). In each case, they occur further downfield than the peaks corresponding to the primary product and other corresponding peaks in structurally characterised 1-substituted products, such as the N-CH_2 methylene peaks in the ^{1}H spectra of (4-phenyldimethylsilyl)butylthymine (**12**) (δ = 3.67ppm) and (4-phenyldimethylsilyl)butylcytosine (**19**) (δ = 3.60 ppm). This is possibly due to the nitrogen in the 3-position being adjacent to two electron withdrawing carbonyl groups, so forming a more polar bond between it and the α-methylene carbon. These minor products are inseparable from the 1-addition products, and are possibly the reason why crystalline samples of the products were not recovered.



20 **20a** **20b** **22a** **23a**

In the case of **20**, a total of three peaks corresponding to methylene protons α to heterocyclic nitrogen were observed. The main peak is observed at δ ~ 3.70 ppm, and corresponds to N^1 addition to thymine, assigned by comparison with the ^1H NMR spectra of 1-butenylthymine (**6**) [δ = 3.78 ppm] and (4-phenyldimethylsilyl)butylthymine (**12**) [δ = 3.67 ppm]. A secondary peak is observed at δ ~ 3.96 ppm, and is thought to correspond to N^3 addition to thymine by comparison with the ^1H NMR spectrum of 1,3-dibutylthymine [δ = 3.90 ppm].[7] A third peak of negligible intensity at δ ~ 4.11 ppm is assumed to correspond to N^3, N^3 addition to thymine. The intensities of the three peaks suggests a **20**:**20a**:**20b** ratio of 25:7:1.

The ^1H and $^{13}C\{1H\}$ NMR data of the alkyl moieties in each of the four products are relatively upfield from their counterparts in the spectra of the (4-phenyldimethylsilyl)butyl-substituted DNA bases discussed in Chapter 4, indicating a less polarised environment for the alkyl chain. This may be due to the higher silicon content in the siloxyalkyl bases than in the "simple" silane-terminated alkyl bases, providing a chemically stabilising effect to the chain, or a less polar environment occurring between the thymine and siloxane groups than between the thymine and silane groups. The ^1H NMR peaks corresponding to the heterocyclic ring proton and methyl group on thymine compare very well those in (4-phenyldimethylsilyl)butylthymine (**11**) (δ = 6.96, 1.91 ppm) and 1-butenylthymine (**6**) (δ = 6.98, 1.92 ppm). The $^{13}C\{^1H\}$ NMR values for the methyl carbons in **22** (δ = 15.9 ppm) and **23** (δ = 15.3 ppm) are similar to **12** (δ = 15.4 ppm), though the values for **20** (δ = 17.4 ppm) and **21** (δ = 17.4 ppm) occur further downfield, and considerably further than in **6** (δ = 12.3 ppm). The peaks in the ^1H NMR spectrum of **21** due to methylene groups are poorly resolved, possibly down to the two alkyl moieties being chemically equivalent and only differentiated

by their rotation about the disiloxane fragment. A spectrum run in a stronger field in a more powerful spectrometer may allow for the peaks to be resolved and assigned, where it might be expected that the peaks due to the methylene groups on the 3-substituted moiety would occur further downfield than those due to the 1-substituted moiety by analogy with the isomers of **20**.

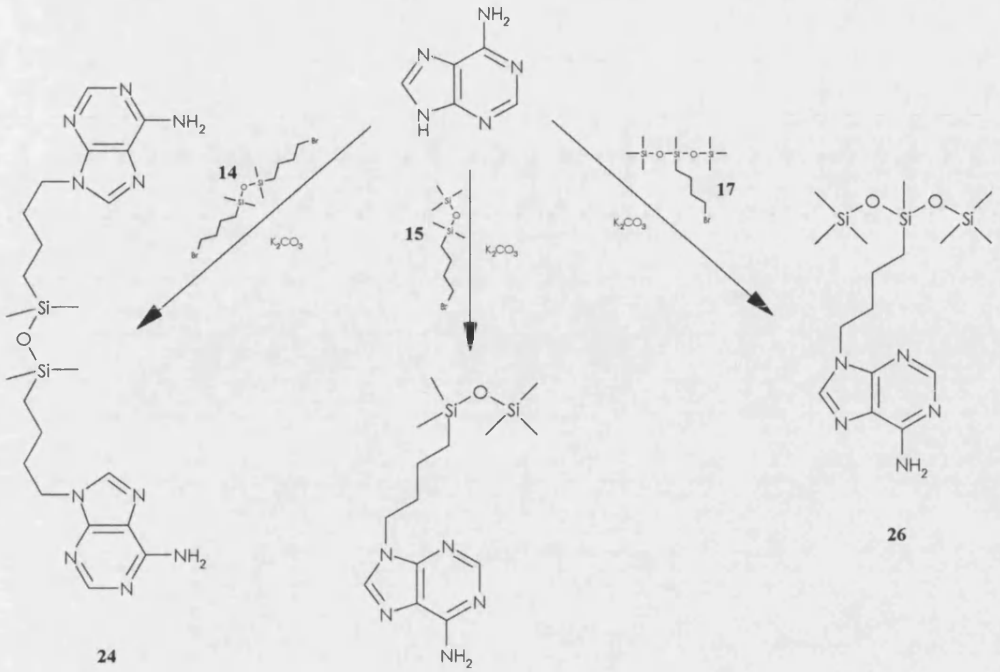
5.3 Substitution of adenine with bromoalkylsiloxanes

A DMSO solution of adenine, potassium carbonate and the appropriate bromoalkylsiloxane (**Scheme 5.3**) was stirred for 72 h, after which a voluminous white, water soluble precipitate had formed in the reaction mixture. The mixture was worked up in the same way as in the analogous reactions with thymine, and gave the corresponding siloxyalkyladenine in each case.

Pertinent reaction data for reactions with adenine is presented in **Table 5.4**. ^{1}H and $^{13}C\{^{1}H\}$ NMR data are presented in **Tables 5.5** and **5.6** respectively.

Table 5.4: Reaction data for substitution of adenine with bromoalkylsiloxanes

	Siloxane Fragment	Yield (%)	Melting Point (°C)
24	TMDS	16	240
25	PMDS	12	181-3
26	HMTS	11	85-7



Scheme 5.3

As with the thymine analogues, the ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of the silylalkyl moieties of the three new compounds are similar, and selected data are presented in **Tables 5.5** and **5.6**. Further data is presented in the experimental section of this chapter.

Table 5.5: ^{1}H NMR data (ppm) for siloxyalkyl adenines

	24	**25**	**26**
Si-C*H*$_2$-CH$_2$- (m, 2H)	0.45	0.47	0.46
Si-CH$_2$-C*H*$_2$- (m, 2H)	1.45	1.24	1.32
-C*H*$_2$-CH$_2$N^9 (m, 2H)	1.79	1.81	1.86
-CH$_2$-C*H*$_2$N^9 (m, 2H)	4.13	4.14	4.14
C$_{Ad}$-*H*	8.33	8.44	8.30
C$_{Ad}$-*H*	7.74	7.93	7.74
N*H*$_2$	7.16	7.09	6.66

Table 5.6: $^{13}C\{^{1}H\}$ NMR data (ppm) for siloxyalkyl adenines

	24	**25**	**26**
Si-*C*H$_2$-CH$_2$-	16.8	16.9	15.2
Si-CH$_2$-*C*H$_2$-	19.5	19.5	18.5
-*C*H$_2$-CH$_2$ N^9	32.5	32.6	31.5
-CH$_2$-*C*H$_2$ N^9	42.2	42.3	41.8

The ^1H NMR data for the alkyl moieties compare relatively well with those of the thymine analogues, with the exception of the peaks due to the methylene protons α to nitrogen, which all occur further downfield than those in the thymine analogues. This may be due to the aromatic secondary amine to which the alkyl moieties in the adenine analogues are bonded exacting a different influence upon the nearest protons when compared to the non-aromatic secondary amine in the thymine analogues. These $N\text{-}CH_2$ resonances compare favourably to the peak due to the α-methylene protons in (4-phenyldimethylsilyl)butyladenine (**18**) (δ = 4.15). The $^{13}C\{^1H\}$ data display further differences to those of the thymine analogues, in the peaks due to the δ-carbon atoms as well as those due to the α-carbons, which both occur further downfield than in the thymine analogues. While the same argument as with the ^1H NMR can be applied to the α-carbon peaks, the peaks due to β- and γ-carbons are similar in the two sets of compounds, so the difference in the δ-carbon peaks cannot be put down to the different type of secondary amine the alkyl moieties are bound to. However, both α-carbon and δ-carbon peaks compare well with those of (4-phenyldimethylsilyl)butyladenine (**18**) (δ = 15.2, 43.4 ppm).

The reactions with adenine have taken place in the same manner as the reactions with thymine, in which **20**, **22** and **23** were prepared. The bromide has substituted with the 9-position, the most basic of the nitrogen positions in adenine,[8] to form a neutral compound in each case. This matches the preferential addition of the bromide to the most basic 1-position in thymine[6] under the same conditions, and is in stark contrast to the unexpected results achieved in the addition of alkenyl bromides to bis-(trimethylsilyl)adenine (**3**), where addition to the 7-position, and even to the 3-position, was observed, and a range of bromide salts were formed. The reaction stoichiometry may contribute to the regiochemistry of the reaction, as in **Scheme.5.3** the DNA base is in excess and the bromoalkane is the limiting reagent, in contrast to the addition of bromoolefins to **3**. It may also be due to the relatively mild conditions employed in this synthesis, causing only the most reactive of the potential sites on the molecule to be involved in the reaction. The products have once again been recovered in low yield, as in the analogous reactions with thymine, possibly due once again to the low solubility of the free base in potential reaction solvents. A significant quantity of white powder was observed remaining uneluted during column chromatography, drawing parallels with the analogous reactions with thymine and suggesting that the reaction did not proceed far towards completion, and possibly that a systematic barrier to reaction is in place for this reaction involving DNA bases in these conditions.

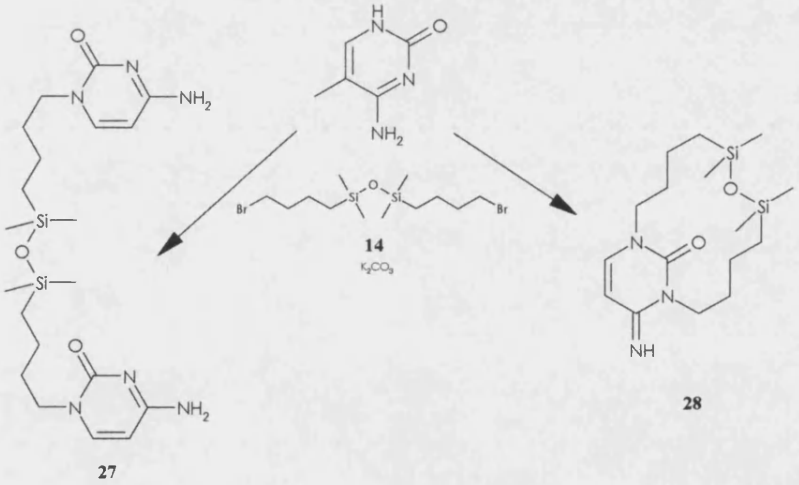
5.4 Substitution of cytosine with 1,3-bis(4-bromobutyl)tetramethyldisiloxane (14)

A DMSO solution of cytosine, potassium carbonate and 1,3-bis(4-bromobutyl)tetramethyldisiloxane (**14**) (**Scheme 5.4**) was stirred for 72 h, after which a voluminous white, water soluble precipitate, very similar to that formed in the reactions with adenine and thymine, had formed in the reaction mixture. The mixture was worked up in the same way as in the analogous reactions with thymine.

Pertinent reaction data for reactions with adenine is presented in **Table 5.7**. ^{1}H and $^{13}C\{^{1}H\}$ NMR data are presented in **Tables 5.8** and **5.9** respectively.

Table 5.7: Reaction data for substitution of cytosine with 1,3-bis(4-bromobutyl)tetramethyldisiloxane (14)

	Yield (%)	Melting Point (°C)
27	9	141-3
28	7	124-7



Scheme 5.4

Predictably, the ^{1}NMR and $^{13}C\{^{1}H\}$ NMR data of the alkyl moieties of the two cytosine compounds bear similarity to each other, and are presented in **Tables 5.8** and **5.9**. Further data is presented in the experimental section.

Table 5.8: ^{1}H NMR data (ppm) for siloxyalkyl cytosines

	27	28
Si-CH_2-CH_2- (m, 2H)	0.51	0.60 (4H)
Si-CH_2-CH_2- (m, 2H)	1.35	1.41 (4H)
-CH_2-CH_2N^1 (m, 2H)	1.74	1.74 (4H)
-CH_2-CH_2N^1 (m, 2H)	4.24	4.19 (m, 4H)

Table 5.9: $^{13}C\{^1H\}$ NMR data (ppm) for siloxyalkyl cytosines

	27	28
Si-CH_2-CH_2-	18.0	16.9
Si-CH_2-CH_2-	20.4	20.2 21.5
-CH_2-CH_2 N^1	32.6	32.3 34.0
-CH_2-CH_2 N^1	50.1	48.7 54.3

27 displays ^{1}H NMR peaks due to the alkyl moieties bearing similarity to its counterpart with thymine (**20**) and (4-phenyldimethylsilyl)butylcytosine (**19**), though the peaks due to the methylene protons α to the nitrogen in **27** are shifted considerably downfield relative to that of **19** (δ = 3.60 ppm) and **20** (δ = 3.70 ppm). The ^{1}H NMR peaks due to the alkyl moieties in **28** are, in similarity to the thymine analogue (**21**), not resolved from each other and appear as overlapping multiplets in every case. They do display strong agreement with the peak positions due to the alkyl moieties in **21**, possibly suggesting a greater chemical similarity between the two fourteen membered ring structures than between **28** and other similar compounds containing N-alkyl moieties bonded to cytosine.

Compound **27** displays $^{13}C\{^1H\}$ NMR peaks due to the alkyl moieties shifted considerably downfield from those in **20** (δ = 12.5, 18.8, 30.9, 39.9 ppm), but comparing very favourably to those of (4-phenyldimethylsilyl)butylcytosine (**19**) (δ = 15.4, 21.0, 32.7, 49.9 ppm). Similarly, **28** displays $^{13}C\{^1H\}$ NMR peaks due to the alkyl moieties comparing much more closely to **19** than to those in the thymine ring compound (**21**) (δ = 12.5, 18.8, 30.9, 39.9), again, the peaks in the cytosine compound appearing much further downfield than those in the corresponding thymine compound.

In a manner similar to the reactions to thymine, 1,3-bis(4-bromobutyl)tetramethyldisiloxane (**14**) has substituted with the free amines on the cytosine in

two ways, both forming neutral compounds containing N-alkyl moieties. Firstly, it reacts with the 1-positions on two molecules of cytosine to form a disubstituted species (**27**). Secondly, it reacts with the 1- and 3-positions on a single molecule of cytosine to form another 14-membered ring structure (**28**), of very similar physical properties to the analogous compound with based on thymine (**21**) but forming an imine in the 4-position. This bears close similarity with the carbonyl group on **21**.

The products formed in this series of reactions with thymine, adenine and cytosine are summarised below. The ^{29}Si NMR data for all compounds is presented in **Table 5.10**.

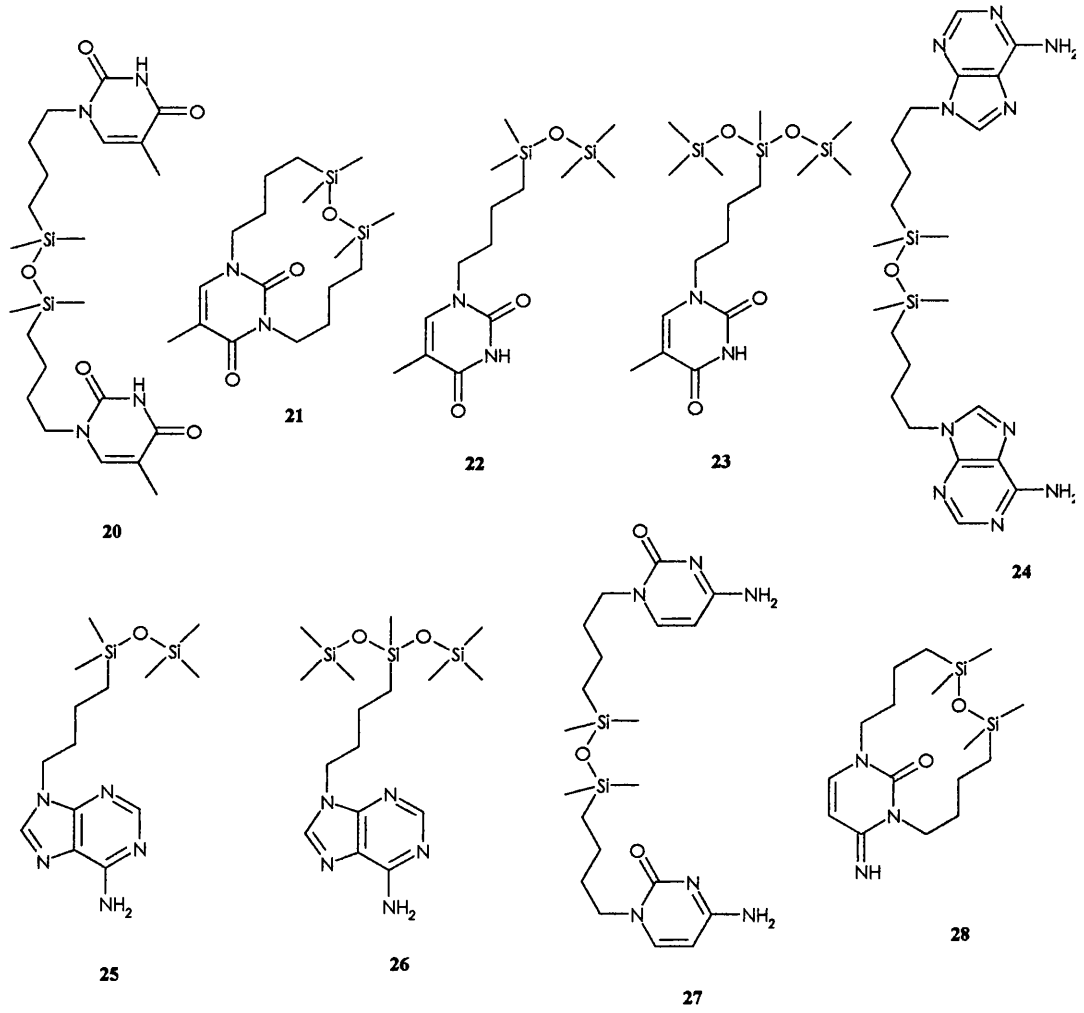


Table 5.10: ^{29}Si NMR data (ppm) for siloxyalkyl DNA bases

	20	21	22	23	24	25	26	27	28
^{29}Si NMR (δ)	6.4 7.1	6.5 7.1	7.0 7.6	-22.3 7.4	6.4 7.0	7.1 7.6	-22.0 7.3	6.5 7.0	6.6 7.1

The data compare relatively well with the ^{29}Si NMR shifts of the three species of siloxane bromides used in their synthesis. The spectra of **20**, **21**, **24**, **27** and **28**, based on 1,3-bis(4-bromobutyl)tetramethyldisiloxane (**14**) display peaks corresponding well with those of **14** (δ = 7.0 ppm), but in contrast to **14**, the two Si centres appear chemically inequivalent on the NMR timescale. This is possibly due to the pendant bases hydrogen bonding with each other and making them chemically non-equivalent, though may also be due more simply to the larger pendant groups in the cases of the siloxyalkyl DNA bases allowing for more rotational asymmetry than the bromoalkyl groups in **14**. This is an area of uncertainty, and further work may be of interest to investigate this inequivalency in what is formally a chemically symmetrical molecule. The spectra of **22** and **25**, based on 1-(4-bromobutyl)-3-phenyltetramethyldisiloxane (**15**), show compare very well with the spectrum of **15** (δ = 7.0, 7.6 ppm). Finally, the spectra of **23** and **26**, based on 3-(4-bromo)butylheptamethyltrisiloxane (**17**), also compare favourably with the spectrum of **17** (δ = 7.5, -22.5 ppm). The peaks due to the trimethylsiloxy groups in the spectra of **22**, **23**, **25** and **26** all occur further downfield than in the spectrum of octamethyltrisiloxane [δ = 7.13 ppm],[9] and the peaks due to the dimethylsiloxy groups in **23** and **26** occur slightly further upfield than in octamethyltrisiloxane [δ = -20.8 ppm].[9]

5.5 Structure of 6,6,8,8,15-Pentamethyl-7-oxa-1,13-diaza-6,8-disila-bicyclo[11.3.1]heptadec-15-ene-14,17-dione (21)

Colourless, tabular crystals of **21** were grown from a solution of the crude products of the reaction between 1,3-bis(4-bromobutyl)tetramethyldisiloxane (**13**) and thymine in DMSO. The molecular structure of **21** is illustrated in **Fig.5.1**. Selected bond lengths and angles are presented in **Tables 5.11** and **5.12**. Crystallographic data is presented in **Appendix 8.12**.

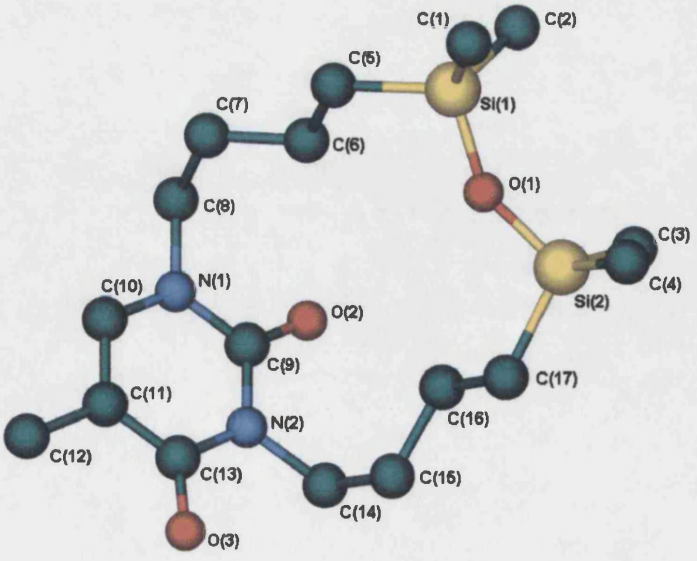


Fig.5.1 Structure of 21

The asymmetric unit of the molecule is a monomer. The two bromide groups have substituted with the heterocyclic ring at the 1- and 3-positions, forming a bis-N-alkyl moiety [N(1)-C(8) 1.475(4), N(2)-C(14) 1.479(4) Å] that describes a 14-membered ring comprised of part of the thymine group, the two alkyl chains and the disiloxane group, oriented above the plane of the thymine ring. The N-C bond distances in the alkyl moieties compare favourably with those of (4-phenyldimethylsilyl)butylthymine (**12**) [1.4777(19) Å], (trimethylsilyl)-1-allylthymine (**11**) [1.475(2) Å, 1.473(2) Å] and 9-allyladeninium chloride hydrate [1.474 Å].[10] The bond distances in the alkyl chains compare also well with those of **12** [C_α-C_β 1.514(2), C_β-C_γ 1.526(2), C_γ-C_δ 1.530(2) Å], though the C-Si distances [C(5)-Si(1) 1.853(3), C(17)-Si(2) 1.862(3) Å] are shorter than those in **12** [C_δ-Si 1.8771(18) Å] and (4-phenyldimethylsilyl)butylcytosine (**19**) [C_δ-Si 1.882(3) Å, 1.869(3) Å].

The bond angles around the two N-alkyl moieties [C(9)-N(1)-C(8) 118.1(2)°, C(9)-N(1)-C(10) 123.6(2)°, C(10)-N(1)-C(8) 118.3(2)°, C(9)-N(2)-C(14) 118.6(2)°, C(9)-N(2)-C(13) 123.5(2)°, C(13)-N(2)-C(14) 117.9(2)°] differ from 120°, indicating a distortion of the ring, opening angles of the heterocyclic amine bonds. This bears similarity with the ring distortion in bis-(trimethylsilyl)thymine (**1**) (N(1)-C(9)-N(2) 127.29(19)°, N(2)-C(5)-C(3) 123.5(2)°), where the bulky trimethylsilyl groups cause the angle at C to distort, opening the angles of the heterocyclic bonds housing the protecting group relative to thymine.[11] The bond angles in the alkyl moieties show differences to those in (4-phenyldimethylsilyl)butylthymine (**12**) and (4-phenyldimethylsilyl)butylcytosine (**19**). The C_α-C_β-C_γ angles in **21** [C(8)-C(7)-C(6) 114.1(3)°, C(14)-C(15)-C(16) 113.9(3)°] are more obtuse than in **12** [110.25(13)°] and **19** [111.95(12)°, 112.71(12)°], and the C_γ-C_δ-Si angles in **21** [C(6)-C(5)-Si(1) 115.3(2)°, C(16)-C(17)-Si(2) 115.0(2)°] are more obtuse than in **12** (113.66(12)°), but more acute than one of the relative bonds in **19** [116.68(12)°]. The Si-O-Si bond angle [Si(1)-O(1)-Si(2) 150.51(15)°] is quite wide, and is a good example of the flexible nature of the siloxane linkage, which can vary between 109° and 180°.[12]

Table 5.11: Selected bond lengths (Å) for 21

N(1)-C(8)	1.475(4)	N(2)-C(14)	1.479(4)
C(8)-C(7)	1.525(4)	C(14)-C(15)	1.524(4)
C(7)-C(6)	1.529(4)	C(15)-C(16)	1.534(4)
C(6)-C(5)	1.537(4)	C(16)-C(17)	1.522(4)
C(5)-Si(1)	1.853(3)	C(17)-Si(2)	1.862(3)
C(9)-O(2)	1.219(3)	C(13)-O(3)	1.267(5)
N(1)-C(9)	1.385(3)	N(2)-C(9)	1.376(4)
N(1)-C(10)	1.391(4)	N(2)-C(13)	1.393(4)
C(10)-C(11)	1.387(5)	C(11)-C(13)	1.386(4)

Table 5.12: Selected bond angles (°) for 21

N(1)-C(8)-C(7)	111.2(3)	N(2)-C(14)-C(15)	112.2(2)
C(8)-C(7)-C(6)	114.1(3)	C(14)-C(15)-C(16)	113.9(3)
C(7)-C(6)-C(5)	113.1(3)	C(15)-C(16)-C(17)	113.2(3)
C(6)-C(5)-Si(1)	115.3(2)	C(16)-C(17)-Si(2)	115.0(2)
C(9)-N(1)-C(8)	118.1(2)	C(9)-N(2)-C(14)	118.6(2)
C(9)-N(1)-C(10)	123.6(2)	C(9)-N(2)-C(13)	123.5(2)
C(10)-N(1)-C(8)	118.3(2)	C(13)-N(2)-C(14)	117.9(2)
C(5)-Si(1)-O(1)	107.96(13)	C(17)-Si(2)-O(1)	107.18(13)
Si(1)-O(1)-Si(2)	150.51(15)	N(1)-C(9)-N(2)	115.2(2)

5.6 16-Imino-6,6,8,8-tetramethyl-7-oxa-1,13-diaza-6,8-disila-bicyclo[11.3.1]heptadec-14-en-17-one (28)

Colourless, tabular crystals of **28** were grown in the same way as in the formation of crystals of **21** above. The molecular structure of **28** is illustrated in **Fig.5.2**. Selected bond lengths and angles are presented in **Tables 5.13** and **5.14**. Crystallographic data is presented in **Appendix 8.13**.

The asymmetric structure of the molecule is a monomer, with no intermolecular interactions. The molecular structure of **28** is very similar to **21**, in that the two bromide groups have substituted with the ring in the 1- and 3-positions, forming a bis-N-alkyl moiety [N(3)-C(11) 1.475(6) Å, N(1)-C(6) 1.494(6) Å], with N-C bond lengths comparing well to those in **21** [1.475(4) Å, 1.479(4) Å], (4-phenyldimethylsilyl)butylthymine (**12**) [1.4777(19) Å] and (trimethylsilyl)-1-allylthymine (**11**) [1.475(2) Å, 1.473(2) Å]. It forms a fourteen membered ring comprising part of the cytosine ring, the two alkyl chains and the disiloxane. The difference lies in the orientation of the moiety with respect to the plane of the heterocyclic ring, which in the case of **28** extends below the plane of the molecule, in contrast to **21** in which the moieties extend above the plane of the ring (**Fig.5.3**).

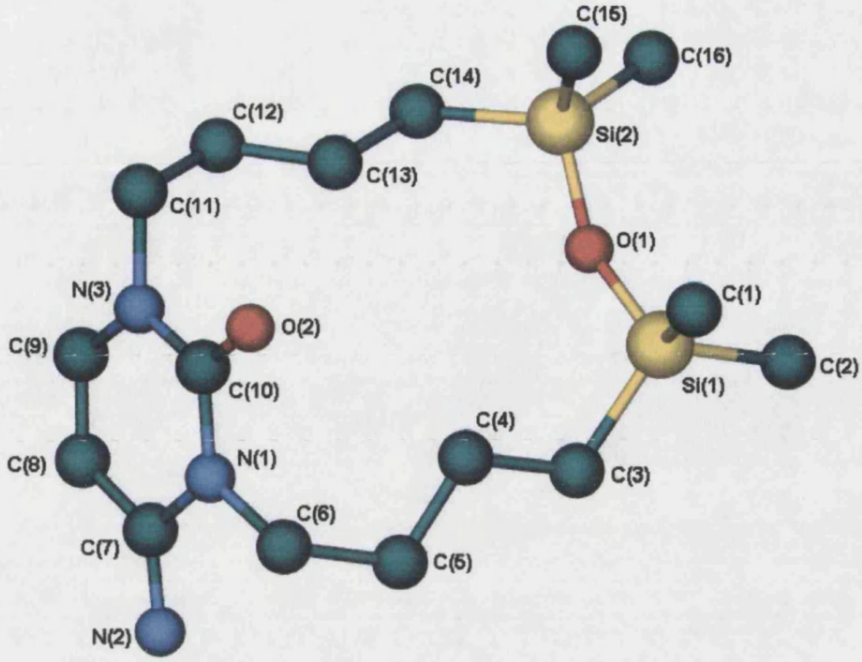


Fig.5.2 Structure of 28

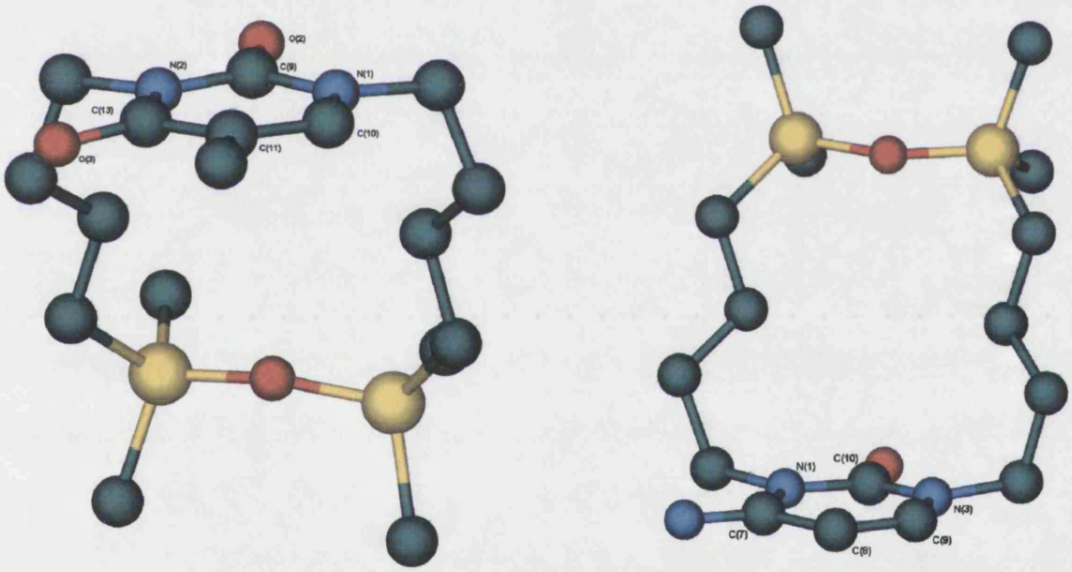


Fig.5.3 Orientation difference between 21 (left) and 28 (right), showing extension of bis-alkyl moiety below the plane of the molecule in 21, and above the plane of the molecule in 28

The bond lengths in the alkyl moieties [N(3)-C(11) 1.475(6) Å, N(1)-C(6) 1.494(6) Å, C(11)-C(12) 1.502(5) Å, C(6)-C(5) 1.544(5) Å, C(12)-C(13) 1.519(3) Å, C(5)-C(4)

1.527(3) Å, C(13)-C(14) 1.531(3) Å, C(4)-C(3) 1.531(3) Å] compare very well with those in **21**, and to a lesser extent with (4-phenyldimethylsilyl)butylthymine (**12**) [C_β-C_γ 1.526(2) Å, C_γ-C_δ 1.530(2) Å] and (4-phenyldimethylsilyl)cytosine (**19**) [C_β-C_γ 1.531(2) Å, 1.530(2) Å, C_γ-C_δ 1.529(2) Å, 1.527(2) Å]. The C-Si distances in **28** [C(14)-Si(2) 1.862(2) Å, C(3)-Si(1) 1.870(2) Å] appear to compare favourably with those in **21** [C(5)-Si(1) 1.853(3) Å, C(17)-Si(2) 1.862(3) Å], though the esds may mask a slight difference in the C-Si bond lengths in the two compounds. The C-Si distance in the 1-position moiety is shorter than that in **12** [1.8771(18) Å].

The bond angles around the N-alkyl moieties in **28** [C(9)-N(3)-C(11) 120.5(4)°, C(9)-N(3)-C(10) 122.3(4)°, C(10)-N(3)-C(11) 117.2(4)°; C(10)-N(1)-C(6) 118.4(4)°, C(10)-N(1)-C(7) 125.0(4)°, C(7)-N(1)-C(6) 116.5(4)°] show a similar distortion from 120° to that in (thymine ring) (**21**), in that the bond angle internal to the heterocyclic ring below the moiety is opened to accommodate the sterically demanding bis-N-alkyl group. In the case of **28**, the distortion occurs to a much greater extent in the 3-position [C(10)-N(1)-C(7) 125.0(4)°] than in the 1-position [C(9)-N(3)-C(10) 122.3(4)°]. The bond angles in the two alkyl moieties in **28** are significantly different to each other in the cases of the N-C_α-C_β and C_α-C_β-C_γ angles [N(3)-C(11)-C(12) 107.5(3)°, C(11)-C(12)-C(13) 112.3(3)°, N(1)-C(6)-C(5) 116.3(3)°, C(6)-C(5)-C(4) 114.2(2)°]. The angle of the N-C_α-C_β bond in the 1-position is considerably more acute and the corresponding bond in the 3-position is considerably more obtuse that those in **21** [111.2(3)°, 112.2(2)°]. The C_α-C_β-C_γ angles in **28** are also more obtuse than in (4-phenyldimethylsilyl)butylthymine (**12**) [110.25(13)°] and (4-phenyldimethylsilyl)-butylcytosine (**19**) [111.95(12)°]. The C_β-C_γ-C_δ angle in the 1-alkyl moiety **28** is relatively similar with that in **21** [113.1(3)°], **12** [114.09(14)°] and **19** [113.15(12)°, 112.63(12)°], whereas the same angle in the 3-alkyl moiety is more obtuse than in **21** [113.2(3)°]. The C_γ-C_δ-Si angles in **28** are more acute than those in **21** [115.3(2)°, 115.0(2)°], though compare well with the relative bond angle in **12** [113.66(12)°]. As in the structure of **21**, the Si-O-Si bond in **28** is wide [S(1)-O(1)-Si(2) 150.38(10)°], displaying great flexibility in the siloxane group and comparing very well with that of **21** [Si(1)-O(1)-Si(2) 150.51(15)°].

Table 5.13: Selected bond lengths (Å) for 28

N(3)-C(11)	1.475(6)	N(1)-C(6)	1.494(6)
C(11)-C(12)	1.502(5)	C(6)-C(5)	1.544(5)
C(12)-C(13)	1.519(3)	C(5)-C(4)	1.527(3)
C(13)-C(14)	1.531(3)	C(4)-C(3)	1.531(3)
C(14)-Si(2)	1.862(2)	C(3)-Si(1)	1.870(2)
C(10)-O(2)	1.174(8)	C(7)-N(2)	1.279(4)
N(3)-C(9)	1.369(5)	N(1)-C(7)	1.418(5)
N(3)-C(10)	1.359(7)	N(1)-C(10)	1.412(6)
C(9)-C(8)	1.339(5)	C(7)-C(8)	1.431(5)

Table 5.14: Selected bond angles (°) for 28

N(3)-C(11)-C(12)	107.5(3)	N(1)-C(6)-C(5)	116.3(3)
C(11)-C(12)-C(13)	112.3(3)	C(6)-C(5)-C(4)	114.2(2)
C(12)-C(13)-C(14)	113.9(2)	C(5)-C(4)-C(3)	114.59(18)
C(13)-C(14)-Si(2)	113.60(16)	C(4)-C(3)-Si(1)	113.44(14)
C(9)-N(3)-C(11)	120.5(4)	C(10)-N(1)-C(6)	118.4(4)
C(9)-N(3)-C(10)	122.3(4)	C(10)-N(1)-C(7)	125.0(4)
C(10)-N(3)-C(11)	117.2(4)	C(7)-N(1)-C(6)	116.5(4)
C(14)-Si(2)-O(1)	107.72(9)	C(3)-Si(1)-O(1)	108.12(9)
S(1)-O(1)-Si(2)	150.38(10)	N(3)-C(10)-N(1)	114.9(4)

5.7 Conclusions

A method has been established for the addition of alkylsiloxanes to DNA bases, though in low yield. The compounds 1,3-bis(1-butylthymine)tetramethyldisiloxane (**20**), 4-pentamethyldisiloxy-1-butylthymine (**22**), 3-(1-butylthymine)heptamethyltrisiloxane (**23**), 1,3-bis(1-butyladenine)tetramethyldisiloxane (**24**), 4-pentamethyldisiloxy-1-butyladenine (**25**), 3-(1-butyladenine)heptamethyltrisiloxane (**26**) and 1,3-bis(1-butylcytosine)tetramethyldisiloxane (**27**) have been synthesised, and characterised by NMR. 14-membered ring species involving thymine (**21**) and cytosine (**28**) have been synthesised, and characterised by X-ray crystallography. Both were found to be monomolecular structures comprising a 14-membered ring consisting of the siloxane group, the two alkyl moieties and part of the thymine group. The method used to synthesise these molecules could be applicable to a siloxane polymer containing pendant 4-bromobutyl groups, indicating a possible synthetic method towards a siloxane polymer with pendant DNA bases at regular intervals. The yields of all the products were low, resulting in part from losses incurred in attempts to purify the products. They are, however, similar to each other in value.

5.8 Experimental

A DMSO solution (40 cm^3) of the DNA base in question, potassium carbonate and the bromoalkylsiloxane in question was stirred at room temperature for 72 h, after which a white precipitate of potassium bromide formed, considerably thickening the solution. The solution was filtered and the residue washed with further DMSO. Data for the amounts of reactants used is presented in **Table 5.15**.

Table 5.15: reaction amounts and yields for the production of siloxyalkyl DNA bases

			Base		Siloxane		K_2CO_3		Yield	
	DNA Base	Siloxane	g	mmol	g	mmol	g	mmol	g	%
20	Thymine	TMDS	0.85	6.72	0.50	1.44	1.11	7.99	0.06	8
21	Thymine	TMDS							0.04	8
22	Thymine	PMDS	1.20	9.54	0.50	1.77	1.57	11.3	0.08	14
23	Thymine	HMTS	0.46	3.65	0.50	1.40	0.62	4.50	0.06	11
24	Adenine	TMDS	0.91	6.72	0.50	1.24	1.11	7.99	0.10	16
25	Adenine	PMDS	1.29	9.54	0.50	1.77	1.57	11.3	0.07	12
26	Adenine	HMTS	0.40	2.96	0.39	1.09	0.48	3.52	0.08	11
27	Cytosine	TMDS	0.75	6.72	0.50	1.24	1.11	7.99	0.05	9
28	Cytosine	TMDS							0.03	7

In the cases of **21** and **28**, the products crystallised spontaneously on standing the filtrate at room temperature for 48 h.

In all other cases (**20**, **22-27**), the DMSO was removed under reduced pressure followed by washing three times with water (50 cm^3). Thin layer chromatography of the resulting white powder, using a mixture of dichloromethane and hexane (98:2), suggested a mixture of three remaining species, at r = 1.00-0.95, 0.70 and 0.65-0.40. Chromatography on silica using the same eluent yielded three bands in each case. The first, eluted with the solvent front, was found to be trace amounts of unreacted siloxane. The second was found to be trace amounts of DMSO, and the third yielded the desired siloxyalkyl DNA base as a white powder. A white powder remaining uneluted was assumed to be the unreacted DNA base. Recrystallisation was attempted from dichloromethane, chloroform, ethyl acetate and a mixture of dichloromethane and hexane, but crystalline samples of the products were not recovered.

1,3-bis(1-butylthymine)tetramethyldisiloxane (**20**): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.57 (bs, 1H, NH), 6.98 (s, 1H, $C_{ar}H$), 3.70 (t, J = 7.0 Hz, 2H, N-C*H*$_2$), 1.92 (s, 3H, C*H*$_3$), 1.70 (m, 2H, NCH_2CH_2), 1.34 (m, 2H, $SiCH_2CH_2$), 0.54 (m, 2H, SiC*H*$_2$), 0.03 (s, 12H, $SiCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.05 (C_{ar}), 151.90(C_{ar}), 137.21 (C_{ar}), 109.37 (C_{ar}), 39.93 (N-*C*H$_2$), 30.88 (NCH_2CH_2), 18.82 ($SiCH_2CH_2$), 17.37 (*C*H$_3$), 12.46 (Si*C*H$_2$), -0.03 ($SiCH_3$); ^{29}Si NMR (60 MHz, $CDCl_3$): δ = 7.08, 6.44; *analysis* calcd for $C_{22}H_{38}N_4O_5Si_2$: C 53.4, H, 7.74, N 11.3 %, found C 52.3, H 7.65, N 10.9 %.

6,6,8,8,15-Pentamethyl-7-oxa-1,13-diaza-6,8-disila-bicyclo[11.3.1]heptadec-15-ene-14,17-dione (**21**): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.99 (s, 1H, $C_{ar}H$), 4.16 (t, J = 7.0 Hz, 4H, N-C*H*$_2$), 1.99 (s, 3H, C*H*$_3$), 1.74 (m, 4H, NCH_2CH_2), 1.35 (m, 4H, $SiCH_2CH_2$), 0.52 (m, 4H, SiC*H*$_2$) 0.07 (s, 12H, $SiCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.05 (C_{ar}), 151.88 (C_{ar}), 137.22 (C_{ar}), 109.36 (C_{ar}), 39.93 (N-*C*H$_2$), 30.89 (NCH_2CH_2), 18.80 ($SiCH_2CH_2$), 17.36 (*C*H$_3$), 12.48 (Si*C*H$_2$), -0.03 ($SiCH_3$); ^{29}Si NMR (60 MHz, $CDCl_3$): δ = 7.14, 6.51; *analysis* calcd for $C_{17}H_{32}N_2O_3Si_2$: C 55.4, H 8.75, N 7.60 %, found C 55.4, H 8.82, N 7.67 %.

4-pentamethyldisiloxy-1-butylthymine (**22**): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.62 (bs, 1H, NH), 7.01 (s, 1H, $C_{ar}H$), 3.68 (t, J = 7.0 Hz, 2H, N-C*H*$_2$), 1.96 (s, 3H, C*H*$_3$), 1.70 (m, 2H, NCH_2CH_2), 1.35 (m, 2H, $SiCH_2CH_2$), 0.54 (m, 2H, SiC*H*$_2$), 0.04 (s, 6H, $SiCH_3$), -0.01 (s, 9H, $SiCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 162.08 (C_{ar}), 148.71 (C_{ar}), 138.44 (C_{ar}), 108.49 (C_{ar}), 39.04 (N-*C*H$_2$), 30.57 (NCH_2CH_2), 18.32 ($SiCH_2CH_2$), 15.94 (*C*H$_3$), 10.35 (Si*C*H$_2$), -1.65 ($SiCH_3$), -1.96 ($SiCH_3$); ^{29}Si NMR (60 MHz, $CDCl_3$): δ = 7.60 ($Si(CH_3)_3$), 7.04; *analysis* calcd for $C_{14}H_{28}N_2O_3Si_2$: C 51.2, H 8.59, N8.62 %, found C 50.7, H 8.32, N 8.62 %.

3-(1-butylthymine)heptamethyltrisiloxane (**23**): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.58 (bs, 1H, NH), 6.96 (s, 1H, $C_{ar}H$), 3.68 (t, J = 7.0 Hz, 2H, N-C*H*$_2$), 1.91 (s, 3H, C*H*$_3$), 1.70 (m, 2H, NCH_2CH_2), 1.35 (m, 2H, $SiCH_2CH_2$), 0.54 (m, 2H, SiC*H*$_2$), 0.10 (s, 18H, $SiCH_3$), 0.09 (s, 3H, $SiCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 162.22 (C_{ar}), 148.79 (C_{ar}), 138.62 (C_{ar}), 108.56 (C_{ar}), 46.67 (N-*C*H$_2$), 30.50 (NCH_2CH_2), 18.29 ($SiCH_2CH_2$), 15.32 (*C*H$_3$), 10.49 (Si*C*H$_2$), -1.85 ($SiCH_3$), -2.13 ($SiCH_3$); ^{29}Si NMR (60 MHz, $CDCl_3$): δ = 7.44 ($Si(CH_3)_3$), -22.3; *analysis* calcd for $C_{16}H_{34}N_2O_4Si_3$: C 47.7, H 8.51, N 6.96 %, found C 46.9, H 8.24, N 6.96 %.

1,3-bis(9-butyladenine)tetramethyldisiloxane (**24**): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.33 (s, 1H, $C_{ar}H$), 7.74 (s, 1H, $C_{ar}H$), 7.16 (bs, 2H, NH_2), 4.13 (t, J = 7.0 Hz, 2H, N-C*H*$_2$), 1.79 (m, 2H, NCH_2CH_2), 1.45 (m, 2H, $SiCH_2CH_2$), 0.45 (m, 2H, SiC*H*$_2$), -0.08 (s, 12H, $SiCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 155.7 (C_{ar}), 152.1 (C_{ar}), 149.3 (C_{ar}), 140.6 (C_{ar}), 118.5 (C_{ar}), 42.2 (N-*C*H$_2$), 32.5 (NCH_2CH_2), 19.5 ($SiCH_2CH_2$), 16.8 (Si*C*H$_2$), -0.12 ($SiCH_3$); ^{29}Si NMR (60

MHz, $CDCl_3$): δ = 6.99, 6.36; *analysis* calcd for $C_{22}H_{36}N_{10}OSi_2$: C 51.5, H 7.08, N 27.3 %, found C 49.8, H 6.94, N 28.4 %.

4-pentamethyldisiloxy-9-butyladenine (**25**): ^1H NMR (300 MHz, $CDCl_3$): δ = 8.44 (s, 1H, $C_{ar}H$), 7.93 (s, 1H, $C_{ar}H$), 7.09 (bs, 2H, NH_2), 4.14 (t, J = 7.0 Hz, 2H, N-CH_2), 1.81 (m, 2H, NCH_2CH_2), 1.24 (m, 2H, $SiCH_2CH_2$), 0.47 (m, 2H, $SiCH_2$), 0.07 (s, 18H, $SiCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 155.8 (C_{ar}), 152.2 (C_{ar}), 149.4 (C_{ar}), 140.6 (C_{ar}), 118.6 (C_{ar}), 42.3 (N-CH_2), 32.6 (NCH_2CH_2), 19.5 ($SiCH_2CH_2$), 16.9 ($SiCH_2$); ^{29}Si NMR (60 MHz, $CDCl_3$): δ = 7.6, 7.1; *analysis* calcd for $C_{14}H_{27}N_5OSi_2$: C 49.8, H 8.06, N 20.8 %, found C 49.3, H 7.93, N 21.7 %.

3-(9-butyladenine)heptamethyltrisiloxane (**26**): ^1H NMR (300 MHz, $CDCl_3$): δ = 8.30 (s, 1H, $C_{ar}H$), 7.74 (s, 1H, $C_{ar}H$), 6.66 (bs, 2H, NH_2), 4.14 (t, J = 7.0 Hz, 2H, N-CH_2), 1.86 (m, 2H, NCH_2CH_2), 1.32 (m, 2H, $SiCH_2CH_2$), 0.46 (m, 2H, $SiCH_2$), 0.07 (s, 18H, $SiCH_3$), 0.06 (s, 3H, $SiCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 155.1 (C_{ar}), 153.0 (C_{ar}), 149.2 (C_{ar}), 140.0 (C_{ar}), 118.6 (C_{ar}), 41.8 (N-CH_2), 31.5 (NCH_2CH_2), 18.5 ($SiCH_2CH_2$), 15.2 ($SiCH_2$), 1.83 ($SiCH_3$), 1.02 ($SiCH_3$); ^{29}Si NMR (60 MHz, $CDCl_3$): δ = 7.32, -22.01; *analysis* calcd for $C_{16}H_{33}N_5O_2Si_3$: C 46.7, H 8.08, N 17.0 %, found C 45.5, H 7.92, N 17.0 %.

1,3-bis(1-butylcytosine)tetramethyldisiloxane (**27**): ^1H NMR (300 MHz, $CDCl_3$): δ = 8.01 (s, 2H, NH_2), 7.10 (d, J = 0.9 Hz, 1H, $C_{ar}H$), 5.78 (d, J = 0.9 Hz, 1H, $C_{ar}H$), 4.24 (t, J = 6.9 Hz, 2H, N-CH_2), 1.74 (m, 2H, NCH_2CH_2), 1.35 (m, 2H, $SiCH_2CH_2$), 0.51 (m, 2H, $SiCH_2$); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 50.1 (N-CH_2), 32.6 (NCH_2CH_2), 20.4 ($SiCH_2CH_2$), 18.0 ($SiCH_2$); ^{29}Si NMR (60 MHz, $CDCl_3$): δ = 7.05, 6.51; *analysis* calcd for $C_{20}H_{36}N_6O_3Si_2$: C 51.7, H 7.81, N 18.1 %, found C 50.8, H 8.49, N 16.9 %.

16-Imino-6,6,8,8-tetramethyl-7-oxa-1,13-diaza-6,8-disila-bicyclo[11.3.1]heptadec-14-en-17-one (**28**): ^1H NMR (300 MHz, $CDCl_3$): δ = 7.13 (d, J = 1.0 Hz, 1H, $C_{ar}H$), 5.92 (d, J = 1.0 Hz, 1H, $C_{ar}H$), 4.19 (t, J = 7.0 Hz, 4H, N-CH_2), 1.74 (m, 4H, NCH_2CH_2), 1.41 (m, 4H, $SiCH_2CH_2$), 0.60 (m, 4H, $SiCH_2$); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 48.74 (N-CH_2), 32.31 (NCH_2CH_2), 20.24 ($SiCH_2CH_2$), 16.94 ($SiCH_2$); ^{29}Si NMR (60 MHz, $CDCl_3$): δ = 7.15, 6.59; *analysis* calcd for $C_{16}H_{31}N_3O_2Si_2$:C 54.4, H 8.44, N 11.9 %, found C 54.1, H 9.33, N 11.9 %.

5.9 References

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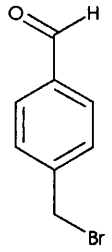
Chapter 6

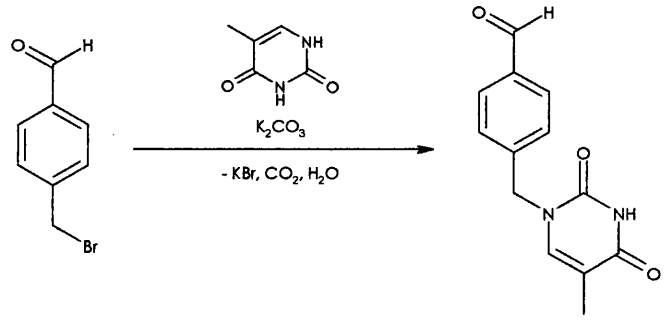
Imine-containing silylalkyl compounds

6.1 Introduction

In addition to the method used to create siloxyalkyl DNA bases in Chapter 5, in which an alkyl bromide is substituted with a free secondary amine on a DNA base and forms an N-alkyl substituted DNA base, other routes are also available. For example, a functionalised DNA base can be reacted with a suitably modified siloxane, potentially aiding in the regulation of the regiochemistry of the siloxane-base linkage by limiting the preferred sites for a link-forming reaction to take place. One such synthesis using this method involves α-bromo-*p*-tolualdehyde.[1]



Substituting this compound with a DNA base such as thymine using the method described in Chapter 5 would afford a product capable of reaction with commercially available amino-functionalised siloxane polymers *via* formation of an imine.

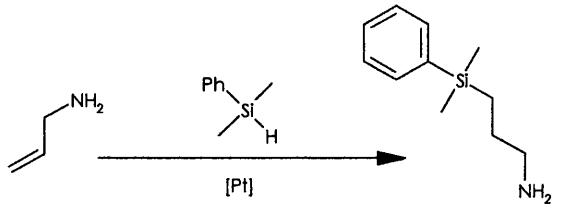


This chapter describes the synthesis of a range of compounds modelling a siloxane polymer with a pendant thymine group *via* a *p*-tolyl imine linkage, and the extension of the method to a siloxane polymer with 2% aminopropyl functionality.

6.2 Hydrosilylation of allylamine with phenyldimethylsilane

The first stage of the investigation involves the formation of a simple amino-functionalised silane to react with the modified thymine group in order to investigate the feasibility of the imine-forming step. (3-phenyldimethylsilyl)aminopropane is a known compound[2] that effectively acts as a model for the aminopropyl-silicone linkage, but has not been extensively characterised.

A mixture of allylamine, phenyldimethylsilane (PhDMS) and a catalytic amount of chloroplatinic acid in propan-2-ol was heated at 90 °C for 18 h until the IR spectrum no longer displayed a peak at 2150 cm^{-1} due to a Si-H stretching vibration, indicating no starting material remained in the reaction mixture. After removal of the volatiles, a translucent oily liquid remained, which was purified by distillation. A colourless, air-stable liquid was recovered and found to be the (3-aminopropyl)phenyldimethylsilane (**29**) (55 %).



29

The silane has added across the double bond to form a tetraorganosilane containing an aminopropyl group in good yield. As in the formation of 4-(phenyldimethylsilyl)-1-bromobutane (**13**), only the ω-silyl isomer has been recovered, suggesting once again that the steric bulk of the silyl group has directed the regiochemistry of the reaction to exclusively produce the "linear" isomer of the product by reacting at the terminal end of the olefin.

The ^1H spectrum of **29** displays a singlet at $\delta = 0.27$ ppm, assigned to the methyl protons attached to silicon. It displays multiplets at $\delta = 0.73$ and 1.43 ppm, assigned to the methylene protons α and β to silicon respectively, and a triplet ($J = 7.0$ Hz) at $\delta = 2.64$ ppm, assigned to the methylene protons α to nitrogen. A singlet at $\delta = 1.17$ ppm was assigned to the amine protons, and multiplets at $\delta = 7.34$ and 7.48 ppm were assigned to the phenyl protons. The peak position of the amine protons is variable due to the level of hydrogen bonding the amine group undergoes with the solvent and other molecules of itself in solution, though the peak in this case was sharp due to the use of a dried chloroform as an NMR solvent. The peaks in the spectrum of **29** due to the α- and β- methylene protons show good agreement

with those of similar molecules such as 4-(phenyldimethylsilyl)-1-bromobutane (**13**) [δ = 0.74, 1.45 ppm].

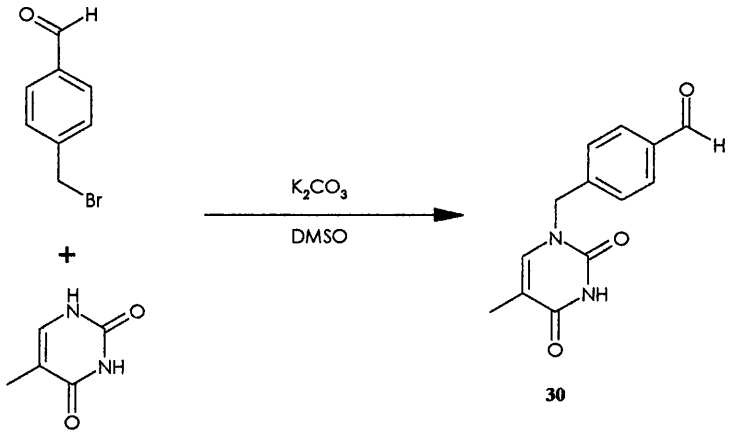
The $^{13}C\{^1H\}$ spectrum of **29** displays a peak at δ = -3.1, assigned to the methyl carbons attached to silicon, and corresponding well with the spectra of similar molecules such as 4-(phenyldimethylsilyl)-1-bromobutane (**13**) [δ = -3.1 ppm]. It also displays peaks at δ = 12.8, 28.2 and 45.5 ppm, assigned to the methylene carbons α, β and γ to silicon respectively. Peaks at δ = 127.7, 128.8, 133.5 and 139.2 were assigned to the phenyl carbons.

The ^{29}Si spectrum of **29** displays a peak at δ = -2.9 ppm, showing good agreement with the corresponding peaks in the spectrum of 4-(phenyldimethylsilyl)-1-bromobutane (**13**) [δ = -3.0 ppm].

6.3 Addition of α-bromo-p-tolualdehyde to thymine

The second stage of the investigation involves the formation of the modified DNA base by the same method used to attach bromoalkylsiloxanes to thymine in Chapter 5.

A DMSO solution of thymine, α-bromo-p-tolualdehyde and an excess of potassium carbonate was stirred at room temperature for 18 h, after which a fine, water soluble precipitate had formed. The mixture was filtered, and the volatiles removed from the filtrate, affording a yellow solid. The solid was washed with water and dried over $MgSO_4$, finely divided and suspended in chloroform, with vigorous stirring, for 1 h. The suspension was filtered, and removal of the volatiles from the filtrate afforded the air-stable product 4-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-ylmethyl)benzaldehyde (**30**) as a yellow powder (88 %, mp 177-9 °C).



30

The ^{1}H NMR spectrum of **30** displays singlets at δ = 1.91 and 4.97, assigned to the protons on the exocyclic methyl group and the methylene protons α to the nitrogen respectively, and a singlet at δ = 7.00, assigned to the proton bonded directly to the thymine ring. It displays doublets (J = 8.0 Hz) at δ = 7.45 and 7.90, assigned to the protons attached to the phenyl group, a broad singlet at δ = 8.91, assigned to the heterocyclic amine proton, and a sharp singlet at δ = 10.02, assigned to the aldehyde proton. The peak due to the methylene protons α to nitrogen compares well with the analogous peak in the ^{1}H NMR spectrum of benzylthymine [δ = 4.87 ppm],[3] indicating similar N^1-subsitution has taken place in the formation of **30**, probably due to the greater basicity of the N^1 position in thymine than the N^3 position.[4]

The $^{13}C\{^1H\}$ NMR spectrum of **30** displays a peak at δ = 12.4, assigned to the exocyclic methyl carbon on thymine, and a peak at δ = 50.9, assigned to the carbon α to the nitrogen. Peaks at δ = 111.8, 139.6, 151.0 and 163.9 were assigned to the carbons in the heterocyclic ring, and peaks at δ = 128.3, 130.5, 136.3 and 142.1 to the carbons in the phenyl group. A peak at 191.5 was assigned to the carbon in the aldehyde group.

6.4 Structure of 30

Thick, faint yellow acicular clusters of crystals of **30** were grown by evaporation of a saturated solution of **30** in dichloromethane. The molecular structure of **30** is illustrated in **Figs.6.1** and **6.2**. Selected bond lengths and angles are presented in **Tables 6.1** and **6.2**. Crystallographic data is presented in **Appendix 8.14**.

The asymmetric unit of the crystal is formed of a single molecule of **30**. *a*-bromo-*p*-tolualdehyde has added to thymine at the nitrogen in the 1-position [N(2)-C(6) 1.475(2) Å] in the manner of the formation of the siloxyalkylthymines in Chapter 5. The N(2)-C(6) distance compares well with N_1-C_α distances in similar molecules such as (trimethylsilyl)-1-allylthymine (**11**) [1.475(2) Å, 1.473(2) Å] and (4-phenyldimethylsilyl)butylthymine (**12**) [1.4777(19) Å]. The C=C double bond [C(2)-C(3) 1.342(3) Å], the endocyclic N_3-C bonds [N(1)-C(1) 1.386(2) Å, N(1)-C(4) 1.375(2) Å] and the endocyclic N_1-C bonds [N(2)-C(3) 1.383(2) Å, N(2)-C(4) 1.367(2) Å] in the thymine ring compare well in length to the analogous bonds in thymine [C(2)-C(3) 1.354(4) Å, N(1)-C(1) 1.403(4) Å, N(1)-C(4) 1.386(4) Å, N(2)-C(3) 1.380(4) Å, N(2)-C(4) 1.386(4) Å],[5] suggesting that little or no ring distortion has taken place in **30** to accommodate the *p*-tolualdehyde group.

The carbon bridge [N(2)-C(6)-C(7) 112.23(13)°] is relatively wide, to accommodate the bulk of the two rings, though the heterocyclic bond angles around the two nitrogen atoms [C(3)-N(2)-C(4) 121.62(14)°, N(1)-C(4)-N(2) 115.01(14)°, C(1)-N(1)-C(4) 126.85(15)°] differ significantly from the analogous angles in thymine [C(3)-N(2)-C(4) 124.1(3)°, N(1)-C(4)-N(2) 112.2(2)°, C(1)-N(1)-C(4) 128.6(3)°].[5] The angles at nitrogen have widened and the angle in between the two nitrogens has narrowed in **30** relative to thymine, indicating a distortion of the ring to accommodate the *p*-tolualdehyde group. The angles around the N^1-C_α bond [C(3)-N(2)-C(6) 119.27(14)°, C(4)-N(2)-C(6) 119.10(14)°, C(3)-N(2)-C(4) 121.62(14)°] compare well with those in (4-phenyldimethylsilyl)butylthymine (**12**) [C(3)-N(2)-C(6) 119.59(13)°, C(4)-N(2)-C(6) 118.76(13)°, C(3)-N(2)-C(4) 121.48(13)°].

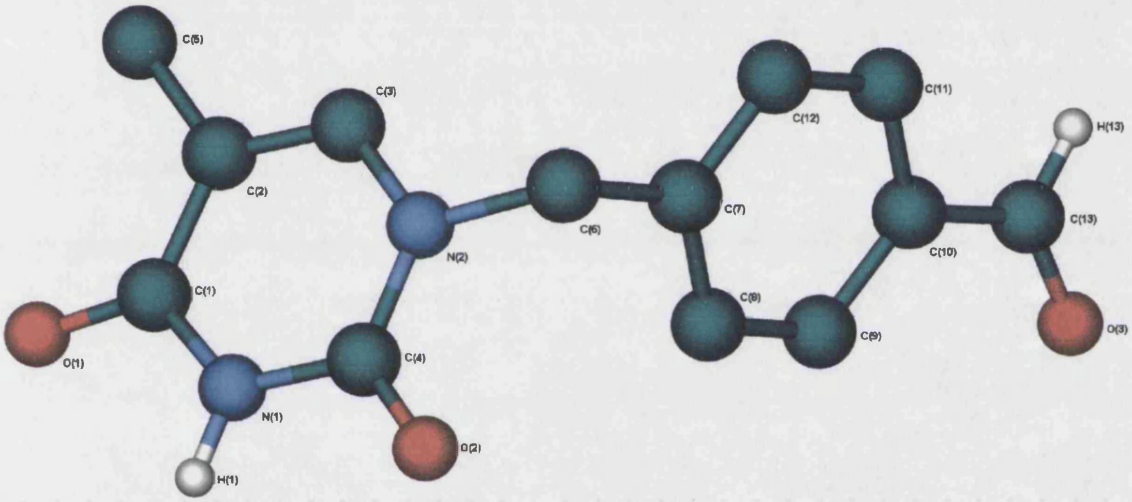


Fig.6.1 Structure of 30

The molecule forms a dimer *via* two symmetry related N-H---O hydrogen bonds [H(1)---O(2) 1.891(3) Å], comparing well in length to similar hydrogen bonds in (4-phenyldimethylsilyl)butylthymine (**12**) [H(1)---O(2) 1.911(10) Å]. They are, however, slightly closer to linearity [N(1)-H(1)---O(2) 176.0(2)] than the analogous bond in **12** [172.77(15)°]. **30** also interacts with itself *via* a C-H---O bond [H(3)---O(3) 2.301(3) Å], longer than analogous bonds in compounds such as 1-methylcytosine [H(1)---O(2) 2.04(2) Å],[6] but similar in length to that found in (trimethylsilyl)-1-allylthymine (**11**) [H(4)---O(3) 2.34(5)]. The bond in **30** is considerably closer to linearity [C(3)-H(3)---O(3) 172.8(2)°] than the analogous bond in **11** [163.9(10)].

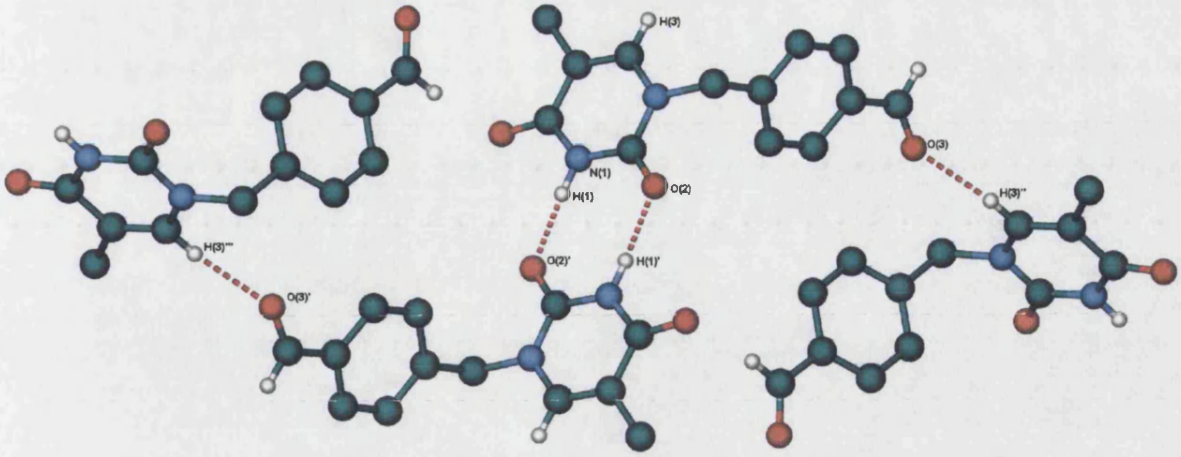


Fig.6.2 Hydrogen bonding patterns in 30

Table 6.1: Selected bond lengths (Å) for 30

N(2)-C(6)	1.475(2)	N(1)-H(1)	0.91(2)
N(2)-C(3)	1.383(2)	C(1)-O(1)	1.226(2)
N(2)-C(4)	1.367(2)	C(4)-O(2)	1.226(2)
C(2)-C(3)	1.342(3)	C(6)-C(7)	1.510(2)
N(1)-C(1)	1.386(2)	C(13)-H(13)	0.95(1)
N(1)-C(4)	1.375(2)	C(13)-O(3)	1.202(2)
H(1)---O(2)	1.891(3)	H(3)---O(3)	2.301(3)

Table 6.2: Selected bond angles (°) for 30

N(2)-C(6)-C(7)	112.2(1)	C(8)-C(7)-C(6)	120.8(2)
C(3)-N(2)-C(6)	119.3(1)	C(12)-C(7)-C(6)	119.8(2)
C(4)-N(2)-C(6)	119.1(11)	C(8)-C(7)-C(12)	119.4(2)
C(3)-N(2)-C(4)	121.6(1)	C(10)-C(13)-O(3)	125.0(2)
C(1)-N(1)-C(4)	126.9(2)	C(10)-C(13)-H(13)	117.5(2)
C(2)-C(3)-N(2)	123.1(2)	O(3)-C(13)-H(13)	117.5(2)
N(1)-H(1)---O(2)	176.0(2)	C(3)-H(3)---O(3)	172.8(2)

6.5 Reaction of (3-aminopropyl)silanes with phenylaldehydes.

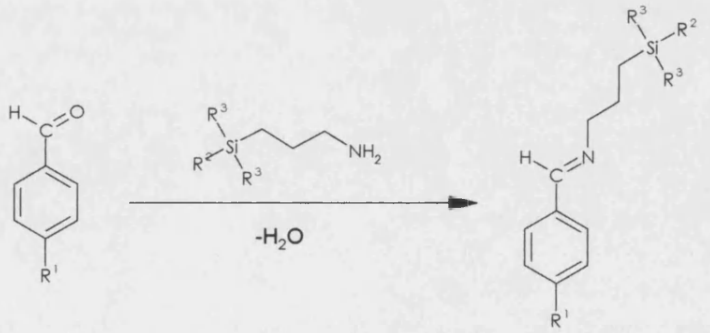
Having established that **30** could be synthesised in good yield and purity, the next stage involved formation of silicon-containing imine compounds modelling a siloxane polymer fragment. (3-phenyldimethylsilyl)aminopropane (**29**) and (3-aminopropyl)-diethoxymethylsilane (obtained commercially) were reacted with benzaldehyde and **30** to form a range of compounds modelling this linkage.

The phenylaldehyde in question was added to a stirred suspension of anhydrous magnesium sulphate in dichloromethane. Once the phenylaldehyde had dissolved, the (3-aminopropyl)silane in question was added and the mixture stirred at room temperature for 18 h, after which the IR spectrum showed no further growth of a peak between 1600 and 1630 cm^{-1}, corresponding to a C=N imine stretching vibration. In the reactions involving benzaldehyde and α-bromo-*p*-tolualdehyde, the reaction was also monitored by observing the IR spectrum of the reaction mixture until there was no longer a peak at 1710 cm^{-1} corresponding to the carbonyl group in the aldehyde. The mixture was filtered and the volatiles removed under reduced pressure to afford the slightly moisture sensitive imine product in each case.

Pertinent data for the reactions are presented in **Table 6.3**.

Table 6.3: Reaction data for formation of iminopropyltriorganosilanes

	Aldehyde	Amine	Yield (%)
31	Benzaldehyde	(3-aminopropyl)phenyldimethylsilane	80
32	Benzaldehyde	(3-aminopropyl)diethoxymethylsilane	60
33	**30**	(3-aminopropyl)phenyldimethylsilane	55
34	**30**	(3-aminopropyl)diethoxymethylsilane	71



R^1 = H, R^2 = Ph, R^3 = Me (31)
R^1 = H, R^2 = Me, R^3 = OEt (32)
R^1 = CH_2T, R^2 = Ph, R^3 = Me (33)
R^1 = CH_2T, R^2 = Me, R^3 = OEt (34)

In each case, the primary amine has reacted with the free aldehyde, eliminating water and forming an imine in good yield and high purity.

The ^{1}H, $^{13}C\{^{1}H\}$ and ^{29}Si NMR spectra for the four compounds are presented in **Tables 6.4-6.6**.

Table 6.4 ^{1}H NMR spectra of iminopropyltriorganosilanes

	31	**32**	**33**	**34**
Si-C*H*$_2$-CH$_2$- (m, 2H)	0.78	0.66	0.74	0.64
Si-CH$_2$-C*H*$_2$- (m, 2H)	1.73	1.79	1.72	1.78
-CH$_2$-C*H*$_2$N$_{imine}$ (t, 2H) (J)	3.58 (7.0 Hz)	3.61 (7.0 Hz)	3.58 (7.0 Hz)	3.61 (6.8 Hz)
***H*C=N (s, 1H)**	8.20	8.26	8.21	8.26
C*H*$_2$N$_{thy}$ (s, 2H)			4.90	4.91
C$_{thy}$-*H* (s, 1H)			6.95	6.96
C$_{thy}$-C*H*$_3$ (s, 3H)			1.88	1.89
Si(C*H*$_3$)$_2$ (s, 6H)	0.28		0.27	
Si-C*H*$_3$ (s, 3H)		0.13		0.13
Si(OC*H*$_2$CH$_3$)$_2$ (q, 4H) (J)		3.76 (7.0 Hz)		3.76 (7.0 Hz)
Si(OCH$_2$C*H*$_3$)$_2$ (t, 6H) (J)		1.21 (7.0 Hz)		1.21 (7.0 Hz)
C$_{Benz}$-*H*	7.33 (m, 3H) 7.70 (d, J = 8.0 Hz, 2H)	7.39 (m, 3H) 7.72 (m, 2H)	7.33 (overlapping m) 7.72 (d, J = 8.0 Hz, 2H)	7.33 (d, J = 8.0 Hz, 2H) 7.74 (d, J = 8.0 Hz, 2H)
C$_{Ph}$-*H*	7.35 (m, 3H) 7.51 (m, 2H)		7.33 (overlapping m) 7.50 (m, 2H)	

The alkyl moieties and the imine proton the four molecules display similar peaks in the ^{1}H NMR spectrum, showing both very good agreement with each other, and similarities to the ^{1}H NMR spectra of analogous molecules such as 4-(phenyldimethylsilyl)-1-bromobutane (**13**) ($\delta_{Si\text{-}CH2}$ = 0.74 ppm). In the spectra of **33** and **34**, the peaks due to the methyl group and ring proton on thymine display good agreement with each other, and similar thymine containing molecules such as 1-butenylthymine (**6**) ($\delta_{Cty\text{-}H}$ = 1.92 ppm, $\delta_{Cty\text{-}CH3}$ = 6.98 ppm) and 3-(1-butylthymine)heptamethyltrisiloxane (**23**) ($\delta_{Cty\text{-}H}$ = 1.91 ppm, $\delta_{Cty\text{-}CH3}$ = 6.96 ppm). The methylene group α to the nitrogen in the 1-position on thymine in both **33** and **34** displays a peak similar to that in **30** ($\delta_{CH2Nthy}$ = 4.97 ppm).

Table 6.5 $^{13}C\{^1H\}$ NMR spectra of iminopropyltriorganosilanes

	31	32	33	34
Si-CH_2-CH_2-	13.3	11.6	12.8	11.0
Si-CH_2-CH_2-	25.4	24.4	22.4	27.2
-CH_2-CH_2N_{imine}	65.0	64.6	64.5	64.6
HC=N	160.9	160.9	160.1	160.2
CH_2N_{thy}			Not Observed	45.1
C_{thy}-CH_3			12.4	12.4
$Si(CH_3)_2$	-3.1		-3.1	
Si-CH_3		-4.9		-4.9
$Si(OCH_2CH_3)_2$		58.2		58.1
$Si(OCH_2CH_3)_2$		18.5		18.4
C_{Benz}	128.0 128.5 130.4 136.3	128.1 128.6 130.5 136.4	128.2 130.0 136.6 142.9	128.2 136.5 143.4
C_{Thy}			111.4 139.6 151.1 163.9	111.4 139.6 151.1 164.0
C_{PhSi}	127.7 128.8 133.6 139.2		127.8 128.8 133.6 139.2	

Once again, the alkyl moieties and imine group in the four molecules display very similar peaks in the $^{13}C\{^1H\}$ NMR spectrum, showing good agreement with spectra of the starting materials (3-phenyldimethylsilyl)aminopropane (**29**) [$\delta_{Si\text{-}CH2}$ = 12.8 ppm, $\delta_{CH2CH2NH2}$ = 28.2 ppm, δ_{CH2NH2} = 45.5 ppm] and (3-aminopropyl)diethoxymethylsilane [$\delta_{Si\text{-}CH2}$ = 11.1 ppm, $\delta_{CH2CH2NH2}$ = 27.4 ppm, δ_{CH2NH2} = 45.6 ppm].

Table 6.6 ^{29}Si NMR spectra of iminopropyltriorganosilanes

	31	32	33	34
Si	-2.9	-4.8	-2.8	-4.6

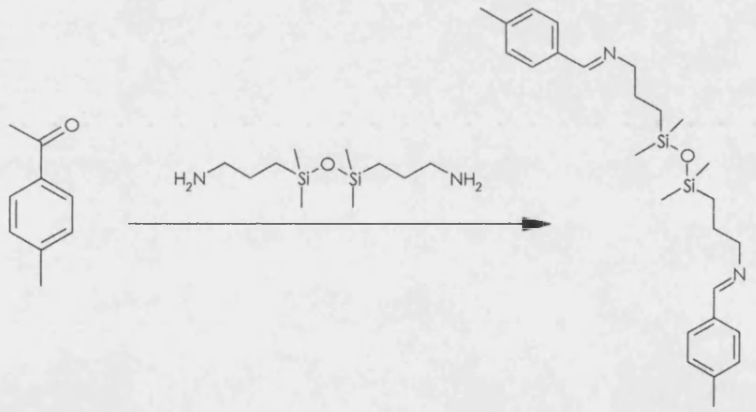
The peaks observed in **31** and **33**, corresponding to a silicon centre surrounded by a phenyl group, two methyl groups and an alkyl group, compare very favourably with analogous peaks observed in the spectra of (4-phenyldimethylsilyl)butylthymine (**12**) (δ = -3.0 ppm), 4-(phenyldimethylsilyl)-1-bromobutane (**13**) (δ = -3.0 ppm) and 2-phenyl-2,6-disilaheptane (δ = -3.0 ppm).[7] The peaks observed in the spectra of **32** and **34** compare

relatively well with the spectrum of the original starting material, (3-aminopropyl)methyldiethoxysilane [δ = -5.0].[8]

6.6 Reaction of 1,3-bis-(3-aminopropyl)tetramethyldisiloxane with paratolualdehyde

Having established the method for forming imines containing a single silane or siloxane, in keeping with the progression of the synthesis involving bromoalkylsiloxanes and DNA bases in Chapters 3-5, the next step was to carry out a imine-forming synthesis using a disiloxane, to more closely model a polymeric structure containing pendant imine groups.

To a stirred suspension of anhydrous magnesium sulphate in dichloromethane was added *p*-tolualdehyde and 3-bis-(3-aminopropyl)tetramethyldisiloxane, and the reaction stirred at room temperature until the IR spectrum no longer displayed a peak at 1710 cm^{-1}, corresponding to a an absence of starting material, and also the appearance of a peak between 1600 and 1630 cm^{-1}, corresponding to a C=N imine stretching vibration. The mixture was filtered, and upon removal of the volatiles from the filtrate the product {3-[1,1,3,3-tetramethyl-3-(3-{[1-*p*-tolyl-meth-(E)-ylidene]-amino}-propyl)-disiloxanyl]-propyl}-[1-*p*-tolyl-meth-(E)-ylidene]-amine (**35**) was afforded as a orange-brown oil (92 %).



35

35 was the only product recovered from the synthesis, and required no further purification. The dimer has reacted with the stoichiometric amount of paratolualdehyde to form a bis-imine compound in very good yield and high purity.

The ^{1}H NMR spectrum of **35** displays a singlet at δ = 0.02 assigned to the methyl protons attached to silicon. It displays multiplets at δ = 0.48 and 1.65, assigned to the methylene protons α and β to the silicon respectively, a singlet at δ = 2.30, assigned to the methyl protons on the tolyl group, and a triplet (J = 7.0 Hz) at δ = 3.50, assigned to the methylene protons γ to the silicon. Two doublets (J = 8.0 Hz) at δ = 7.14 and 7.54 were assigned to the aromatic tolyl protons, and a singlet at δ = 8.14 was assigned to the imine proton.

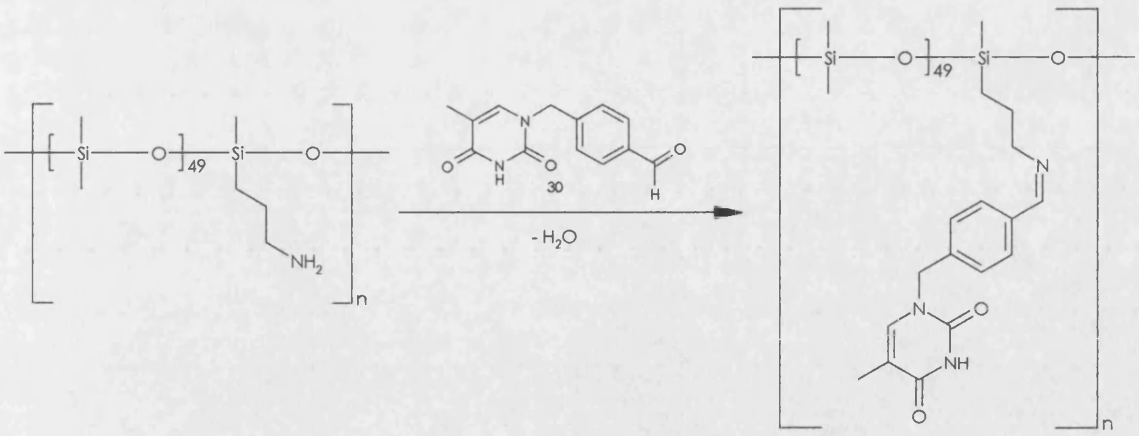
The $^{13}C\{^{1}H\}$ NMR spectrum of **35** displays a peak at δ = -0.4, assigned to the methyl carbons attached to silicon. It also displays peaks at δ = 15.7 and 21.1, assigned to the carbons α and β to the silicon respectively, a peak at δ = 24.5, assigned to the methyl carbon in the tolyl group, and a peak at δ = 64.5, assigned to the carbon γ to the silicon. Peaks at δ = 127.7, 128.9, 133.4 and 140.2 were assigned to the carbons in the phenyl group, and a peak at δ = 160.3 was assigned to the imine carbon.

The ^{29}Si spectrum of **35** displays a peak at δ = 7.7 ppm, corresponding relatively well to the analogous peak in the spectrum of 1,3-bis(4-bromobutyl)tetramethyldisiloxane (**14**) [δ = 7.0 ppm] and 1,3-bis(1-butylthymine)tetramethyldisiloxane (**20**) [δ = 6.4, 7.1 ppm].

The final stage of the synthesis was to attempt to use the imine-forming reaction to form a siloxane polymer containing pendant DNA bases. A PDMS containing 2% aminopropyl functionality, obtained from Dow Corning, was used with **30**, employing the same method used to form the model compounds described in this chapter.

6.7 Reaction between PDMS (2 % aminopropyl) and 30

30 was added to a stirred suspension of anhydrous magnesium sulphate in dichloromethane and allowed to dissolve. To this was added PDMS containing 2 % aminopropyl functionality, and the mixture was stirred at room temperature for 18 h, after which the mixture had visibly thickened and no further growth in a peak between 1600 and 1630 cm^{-1}, corresponding to a C=N imine stretching vibration, was observed in the IR spectrum. The mixture was further diluted with dichloromethane before being filtered and dried over anhydrous magnesium sulphate. Upon removal of the volatiles a very thick, air stable yellow rubber was recovered and found to be PDMS containing approximately 2 % iminopropylthymine functionality (**36**) *via* a propyl imine linkage.



36

It is interesting to note that **36** is not significantly air or moisture sensitive. The chemical stability of the siloxane chain and the conjugation of the imine with the benzyl group serve to protect the moisture sensitive imine group and form a polymer stable to air over the course of several months.

The ^{1}H NMR spectrum of **36** displays a large peak at $\delta = 0.26$ ppm, corresponding to methyl protons attached to silicon. Other peaks were faint and poorly resolved due to the relatively low intensity of the signals in comparison to the methyl silicon protons, though peaks are observable at $\delta = 0.8$, 1.6 and 3.6 ppm, corresponding to the methylene protons α, β and γ to silicon respectively. Peaks at $\delta = 1.9$ and 6.96 ppm were assigned to the methyl group attached to thymine and the heterocyclic ring proton respectively, and peaks at $\delta = 7.02$ and 7.11 ppm were assigned to the protons in the phenyl group of the pendant group. A peak at $\delta = 8.05$ was assigned to the imine proton. These values compare well with those in the spectrum of the model compound **34**, indicating that as with the formation of the model compounds, the aldehyde group of **30** has reacted with the amine group on the siloxane polymer to form an imine, linking the thymine to the siloxane chain, though the peak due to the imine proton is slightly further upfield in the spectrum of **36** than in that of **34** [$\delta = 8.26$ ppm].

The $^{13}C\{^{1}H\}$ NMR spectrum of **36** displays a peak at $\delta = 1.4$ ppm, corresponding to the methyl carbons attached to silicon. No other peaks were observed, probably due to the low sensitivity of ^{13}C spectra relative to ^{1}H spectra, and the PDMS methyl groups existing in much higher concentration than the pendant group.

The ^{29}Si NMR spectrum of **36** displays a peak at δ = -21.5, corresponding well to other examples of dimethylsiloxy groups such as those in octamethyltrisiloxane [O_2SiMe_2 δ = -20.8].[9]

The number average molecular weight of **36**, derived by gel permeation chromatography, is 21,000, with a polydispersity of 3.6, indicating that the grafting of **30** onto the aminopropyl functionalised PDMS has resulted in a stable siloxane polymer. The molecular weight of the repeat unit of PDMS is 74, suggesting that **36** has a chain structure containing the order of a few hundred repeat units.

Preliminary DSC and X-ray scattering experiments on samples of **36** suggest that there may be physical interactions present in the solid state, presumably in the form of hydrogen bonding between the pendant thymine molecules, though time constraints prevented a more detailed investigation. It is therefore of interest to carry out a more thorough analysis of the physical properties of **36**, in order to understand the influences the pendant DNA bases place upon the siloxane chain.

6.8 Conclusions

A range of compounds have been synthesised modelling an imine linkage between silicon and thymine, and a siloxane polymer with a known level of aminopropyl functionality has been used in conjunction with functionalised thymine, to form a siloxane polymer containing a known amount of thymine *via* a pendant group containing a benzyl imine (**36**).

The compounds (3-phenyldimethylsilyl)-1-aminopropane (**29**), 4-(5-Methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-ylmethyl)-benzaldehyde (**30**), [3-(Dimethyl-phenyl-silanyl)-propyl]-[1-phenyl-meth-(E)-ylidene]-amine (**31**), [3-(Diethoxy-methyl-silanyl)-propyl]-[1-phenyl-meth-(E)-ylidene]-amine (**32**), [1-(4-Bromomethyl-phenyl)-meth-(E)-ylidene]-[3-(dimethyl-phenyl-silanyl)-propyl]-amine (**33**), [1-(4-Bromomethyl-phenyl)-meth-(E)-ylidene]-[3-(diethoxy-methyl-silanyl)-propyl]-amine (**34**), 1-(4-{[(E)-3-(Dimethyl-phenyl-silanyl)-propylimino]-methyl}-benzyl)-5-methyl-1*H*-pyrimidine-2,4-dione (**33**), 1-(4-{[(E)-3-(Diethoxy-methyl-silanyl)-propylimino]-methyl}-benzyl)-5-methyl-1*H*-pyrimidine-2,4-dione (**34**) and {3-[1,1,3,3-Tetramethyl-3-(3-{[1-*p*-tolyl-meth-(E)-ylidene]-amino}-propyl)-disiloxanyl]-propyl}-[1-*p*-tolyl-meth-(E)-ylidene]-amine (**35**) have been synthesised and characterised by NMR. **30** has also been characterised by X-ray diffraction, and forms a dimer *via* two symmetry related N-H---O hydrogen bonds, and an extended structure *via* a C-

H---O bond. A PDMS polymer has been synthesised containing 2% pendant thymine functionality *via* a benzylimine linking group (**36**).

While a siloxane polymer containing a pendant DNA base a regular intervals has been synthesised, there is a significant distance between the base functionality and the siloxane chain. It remains of interest to attempt to formulate further PDMS compounds with the base connected to the backbone *via* a shorter pendant chain.

6.9 Experimental

6.2 Hydrosilylation of allylamine with phenyldimethylsilane

Allylamine (2.3 g, 53 mmol), phenyldimethylsilane (PhDMS) (2.5 g, 18.3 mmol) and a catalytic amount of chloroplatinic acid in propan-2-ol was heated at 90 °C for 18 h, after which the IR spectrum no longer displayed a peak at 2150 cm^{-1} due to a Si-H stretching vibration. The volatiles were removed under reduced pressure and the resulting translucent grey liquid distilled under atmospheric pressure. The only product recovered was found to be (3-aminopropyl)phenyldimethylsilane (**29**) (55 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.48 (m, 2H, $C_{Ph}H$), 7.34 (m, 3H, $C_{Ph}H$), 2.64 (t, J = 7.0 Hz, 2H, CH_2NH_2), 1.43 (m, 2H, Si-CH_2CH_2), 1.17 (s, 2H, NH_2), 0.73 (m, 2H, Si-CH_2), 0.27 (s, 6H, Ph(CH_3)$_2$Si); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 139.2 (C_{Ph}), 133.5 (C_{Ph}), 128.9 (C_{Ph}), 127.7 (C_{Ph}), 45.5 (CH_2NH_2), 28.2 ($CH_2CH_2NH_2$), 12.8 (Si-CH_2), -3.1 (Ph(CH_3)$_2$Si); ^{29}Si NMR (60 MHz, $CDCl_3$): δ = -2.9; *analysis* calcd for $C_{11}H_{19}NSi$: C 68.3, H 9.90, N 7.20 %, found C 67.8, H 9.90, N 7.20 %.

6.3 Addition of α-bromo-p-tolualdehyde to thymine

A solution of thymine (2.0 g, 5 mmol), α-bromo-*p*-tolualdehyde (1.04 g. 5.2 mmol) and an excess of potassium carbonate in DMSO was stirred at room temperature for 18 h, after which a fine, voluminous precipitate had formed in the reaction mixture. The mixture was filtered and the excess DMSO was removed from the filtrate, affording a slightly oily yellow solid. The solid was washed with water and dried over anhydrous magnesium sulphate, finely divided with a pestle and mortar and suspended in chloroform, with vigorous stirring, for 1 h. The suspension was filtered, and removal of the excess chloroform from the filtrate afforded the air-stable product 4-(5-Methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-ylmethyl)-benzaldehyde (**30**) as a fine yellow powder (88 %, mp 177-9 °C). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 10.02 (s, 1H, C*H*O), 8.91 (bs, 1H, N-*H*), 7.90 (d, J = 8.0 Hz, 2H, $C_{Ph}H$), 7.45 (d, J = 8.0 Hz, $C_{Ph}H$), 7.00 (s, 1H, C_{ty}-*H*), 4.97 (s, 2H, N-CH_2), 1.91 (s, 3H, C_{ty}-CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 191.5 (*C*HO) 163.9 (C_{Ty}), 151.0 (C_{Ty}), 142.1 (C_{Ph}), 139.6 (C_{Ty}),

130.5 (C_{Ph}), 128.3 (C_{Ph}), 111.8 (C_{Ty}), 50.9 (N-CH_2), 12.4 (C_{ty}-CH_3); *analysis* calcd for $C_{13}H_{12}O_3N_2$: C 63.9, H 4.95, N 11.5 %, found C 63.5, H 4.91, N 11.1 %.

6.5 Reaction of (3-aminopropyl)silanes with phenylaldehydes.

The phenylaldehyde in question was added to a stirred suspension of anhydrous magnesium sulphate in dichloromethane. Once the phenylaldehyde had dissolved, the (3-aminopropyl)silane in question was added and the mixture stirred at room temperature for 18 h, after which the IR spectrum revealed an absence of starting material. Pertinent details of reaction amounts and yields are displayed in **Table 6.7**

Table 6.7 Reaction data for formation of iminopropyltriorganosilanes

			Aldehyde		Amine		DCM	Yield	
	Aldehyde	**Amine**	g	mmol	g	mmol	ml	g	%
31	Benzaldehyde	Mono	0.32	3.02	1.00	5.17	50	0.68	80
32	Benzaldehyde	Poly	0.32	3.02	1.00	5.23	50	0.51	60
33	**30**	Mono	0.21	0.86	0.26	1.36	50	0.20	55
34	**30**	Poly	0.74	3.02	0.57	3.02	30	0.90	71

The mixture was filtered and the excess dichloromethane removed under reduced pressure to afford the slightly moisture sensitive imine product in each case, requiring no further purification.

[3-(Dimethyl-phenyl-silanyl)-propyl]-[1-phenyl-meth-(E)-ylidene]-amine (**31**): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.20 (s, 1H, *H*C=N), 7.70 (d, J = 8.0 Hz, 2H, $C_{Benz}H$), 7.51 (m, 2H, $C_{Ph}H$), 7.35 (m, 3H, $C_{Ph}H$), 7.33 (m, 3H, $C_{Benz}H$), 3.58 (t, J = 7.0 Hz, 2H, CH_2N=CH), 1.73 (m, 2H, Si-CH_2-CH_2-), 0.78 (m, 2H, Si-CH_2-CH_2-), 0.28 (s, 6H, Si(CH_3)$_2$); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 160.9 (HC=N), 139.2 (C_{Ph}), 136.3 (C_{Benz}), 133.6 (C_{Ph}), 130.4 (C_{Benz}), 128.8 (C_{Ph}), 128.5 (C_{Benz}), 128.0 (C_{Benz}), 127.7 (C_{Ph}), 65.0 (CH_2N=CH), 25.4 (Si-CH_2-CH_2-), 13.3 (Si-CH_2-CH_2-), -3.1 (Si(CH_3)$_2$); ^{29}Si NMR (60 MHz, $CDCl_3$): δ = -2.9; *analysis* calcd for $C_{18}H_{23}NSi$: C 76.8, H 8.24, N 4.98 %, found C 76.2, H 8.30, N 5.0 %.

[3-(Diethoxy-methyl-silanyl)-propyl]-[1-phenyl-meth-(E)-ylidene]-amine (**32**): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.26 (s, 1H, *H*C=N), 7.72 (m, 2H, $C_{Benz}H$), 7.36 (m, 3H, $C_{Benz}H$), 3.76 (q, J = 7.0 Hz, 4H, Si(OCH_2CH_3)$_2$), 3.61 (t, J = 7.0 Hz, 2H, CH_2N=CH), 1.79 (m, 2H, Si-CH_2-CH_2-), 1.21 (t, J = 7.0 Hz, 6H, Si(OCH_2CH_3)$_2$), 0.66 (m, 2H, Si-CH_2-CH_2-), 0.13 (s, 3H, SiCH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 160.9 (HC=N), 136.4 (C_{Benz}), 130.5 (C_{Benz}), 128.6

(C_{Benz}), 128.1 (C_{Benz}), 64.6 (CH_2N=CH), 58.2 (Si(OCH_2CH_3)$_2$), 24.4 (Si-CH_2-CH_2-), 18.5 (Si(OCH_2CH_3)$_2$) 11.6 (Si-CH_2-CH_2-), -4.9 ($SiCH_3$); ^{29}Si NMR (60 MHz, $CDCl_3$): δ = -4.8; *analysis* calcd for $C_{15}H_{25}O_2NSi$: C 64.5, H 9.02, N 5.01 %, found C 65.2, H 8.90, N 5.0 %.

1-(4-{[(E)-3-(Dimethyl-phenyl-silanyl)-propylimino]-methyl}-benzyl)-5-methyl-1*H*-pyrimidine-2,4-dione (**33**): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.21 (s, 1H, *H*C=N), 7.72 (d, J = 8.0 Hz, 2H, $C_{Benz}H$), 7.50 (m, 2H, $C_{Ph}H$), 7.33-5 (m, 4H, $C_{Ph}H$/$C_{Benz}H$), 6.95 (s, 1H, $C_{thy}H$), 4.90 (s, 2H, CH_2N_{thy}), 3.58 (t, J = 7.0 Hz, 2H, CH_2N=CH), 1.88 (s, 3H, $C_{thy}CH_3$), 1.72 (m, 2H, Si-CH_2-CH_2-), 0.74 (m, 2H, Si-CH_2-CH_2-), 0.27 (s, 6H, Si(CH_3)$_2$); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 161.9 (C_{thy}), 160.1 (HC=N), 150.0 (C_{thy}), 142.9 (C_{Benz}), 139.6 (C_{thy}), 139.2 (C_{Ph}) 136.6 (C_{Benz}), 133.6 (C_{Ph}), 130.0 (C_{Benz}), 128.8 (C_{Ph}), 128.2 (C_{Benz}), 127.8 (C_{Ph}), 111.4 (C_{thy}), 64.5 (CH_2N=CH), 22.4 (Si-CH_2-CH_2-), 12.8 (Si-CH_2-CH_2-), 12.4 ($C_{thy}CH_3$), -3.1 (Si(CH_3)$_2$); ^{29}Si NMR (60 MHz, $CDCl_3$): δ = -2.8; *analysis* calcd for $C_{24}H_{29}N_3O_2Si$: C 68.7, H 6.97, N 10.0 %, found C 68.2, H 6.9, N 9.9 %.

1-(4-{[(E)-3-(Diethoxy-methyl-silanyl)-propylimino]-methyl}-benzyl)-5-methyl-1*H*-pyrimidine-2,4-dione (**34**): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.26 (s, 1H, *H*C=N), 7.74 (d, J = 8.0 Hz, 2H, $C_{Benz}H$), 7.33 (d, J = 8.0 Hz, 2H, $C_{Benz}H$), 6.96 (s, 1H, $C_{thy}H$), 4.91 (s, 2H, CH_2N_{thy}), 3.76 (q, J = 7.0 Hz, Si(OCH_2CH_3)$_2$) 3.61 (t, J = 6.8 Hz, 2H, CH_2N=CH), 1.89 (s, 3H, $C_{thy}CH_3$), 1.78 (m, 2H, Si-CH_2-CH_2-), 1.21 (t, J = 7.0 Hz, 6H, Si(OCH_2CH_3)$_2$), 0.64 (m, 2H, Si-CH_2-CH_2-), 0.13 (s, 3H, $SiCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.0 (C_{thy}), 160.2 (HC=N), 151.1 (C_{thy}), 143.4 (C_{Benz}), 139.6 (C_{thy}), 136.5 (C_{Benz}), 128.2 (C_{Benz}), 111.4 (C_{thy}), 64.6 (CH_2N=CH), 58.1 (Si(OCH_2CH_3)$_2$), 27.2 (Si-CH_2-CH_2-), 18.4 (Si(OCH_2CH_3)$_2$) 11.0 (Si-CH_2-CH_2-), -4.9 ($SiCH_3$); ^{29}Si NMR (60 MHz, $CDCl_3$): δ = -4.6; *analysis* calcd for $C_{24}H_{29}N_3O_2Si$: C 60.3, H 7.71, N 10.0 %, found C 60.1, H 7.7, N 9.9 %.

6.6 Reaction of 1,3-bis-(3-aminopropyl)tetramethyldisiloxane with paratolualdehyde

To a stirred suspension of anhydrous magnesium sulphate in dichloromethane was added paratolualdehyde and 3-bis-(3-aminopropyl)tetramethyldisiloxane, and the reaction stirred at room temperature until the IR spectrum revealed an absence of starting material. The mixture was filtered, and upon removal of the excess dichloromethane from the filtrate the product {3-[1,1,3,3-Tetramethyl-3-(3-{[1-*p*-tolyl-meth-(E)-ylidene]-amino}-propyl)-disiloxanyl]-propyl}-[1-*p*-tolyl-meth-(E)-ylidene]-amine (**35**) was afforded as a orange-brown oil (92 %) with no further purification. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.14 (s, 1H, *H*C=N), 7.54 (d, J = 8.0 Hz, 2H, $C_{Ph}H$), 7.14 (d, J = 8.0 Hz, 2H, $C_{Ph}H$), 3.50 (t, J = 7.0 Hz, 2H,

CH_2N=CH), 2.30 (s, 3H, $C_{Ph}CH_3$), 1.65 (m, 2H, Si-CH_2-CH_2-CH_2-), 0.48 (m, 2H, Si-CH_2-CH_2-), 0.02 (s, 12H, $SiCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 160.2 (HC=N), 140.2 (C_{Ph}), 133.4 (C_{Ph}), 128.9 (C_{Ph}), 127.7 (C_{Ph}), 64.5 (CH_2N=CH), 24.5 ($C_{Ph}CH_3$), 21.1 (Si-CH_2-CH_2-), 15.7 (Si-CH_2-CH_2-), -0.4 ($SiCH_3$); ^{29}Si NMR (60 MHz, $CDCl_3$): δ = 7.7; *analysis* calcd for $C_{26}H_{40}N_2Si_2O$: C 69.0, H 8.9, N 6.2 %, found C 68.8, H 8.8, N 6.2 %.

6.7 Reaction between PDMS (2 % aminopropyl) and 30

30 was added to a stirred suspension of anhydrous magnesium sulphate in dichloromethane and allowed to dissolve. To this was added PDMS containing 2 % aminopropyl functionality, and the mixture was stirred at room temperature for 18 h, after which the mixture had visibly thickened and the IR spectrum displayed no further formation of product. The mixture was further diluted with dichloromethane before being filtered, washed with a small amount of water and dried over anhydrous $MgSO_4$. Upon removal of the volatiles a very thick, air stable yellow rubber was recovered and found to be PDMS containing approximately 2 % iminopropylthymine functionality (**36**) *via* a propyl imine linkage. ^{1}H NMR (300 MHz, $C_6D_5CD_3$): δ = 8.05 (s, 1H, HC=N), 7.11 ($C_{Ph}H$), 7.02 ($C_{Ph}H$), 3.6 (t, J = 7.0 Hz, 2H, CH_2N=CH), 1.9 (s, 3H, $C_{thy}CH_3$), 1.6 (m, 2H, Si-CH_2-CH_2-), 0.8 (m, 2H, Si-CH_2-CH_2-), 0.26 (s, ~ 300H, $SiCH_3$); ^{13}C NMR (75 MHz, $C_6D_5CD_3$): δ = 1.4 ($SiCH_3$); ^{29}Si NMR (60 MHz, $C_6D_5CD_3$): δ = -21.5; *analysis* found C 31.7, H 7.64, N 0.69 %; GPC: Mn 21,000, Mw/Mn 3.6.

6.10 References

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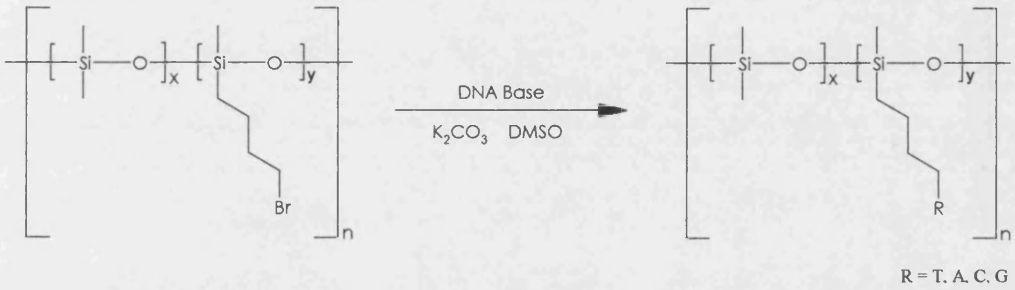
Chapter 7

Siloxane polymers with pendant DNA bases

7.1 Introduction

In Chapter 6 it was shown that a siloxane polymer with DNA bases at regular intervals could be synthesised by the use of a benzylimine linking group between the DNA base and the polymer chain. In order to form a polymer containing a shorter pendant group, a more direct reaction between polymer and base is required. If the method used to form DNA bases with pendant siloxanes in Chapter 5 were extended, a bromoalkyl functionalised siloxane polymer could be reacted with the DNA base and form a polymer with pendant bases much closer to the polymer backbone than the example in Chapter 6.



A suitable bromoalkyl functionalised siloxane polymer, containing a tuneable degree of functionality is required. Reaction of a dimethylsiloxane oligomer of known molecular weight with varying amounts of (4-bromobutyl)heptamethyltrisiloxane (**17**) might allow for a range of suitable polymer precursors, and subsequently a range of DNA base containing polymers, to be synthesised, allowing their physical properties to be investigated.

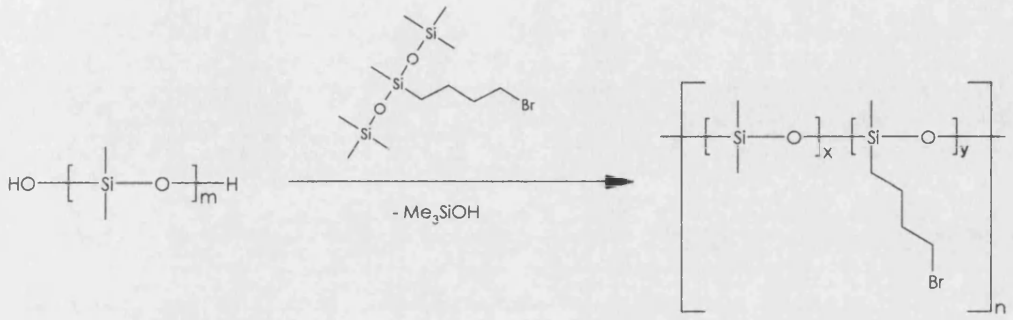
This chapter briefly describes the synthesis of siloxane polymers with varying concentrations of bromobutyl functionality, their subsequent reaction with DNA bases, and the characterisation of the products.

7.2 Formation of bromobutyl functionalised PDMS

The first stage in the synthesis involved the reaction of 3-(4-bromo)butylheptamethyltrisiloxane (**17**) with polymers of known approximate molecular weight to form siloxane polymers with approximately known concentrations of pendant bromobutyl groups.

A mixture of 3-(4-bromo)butylheptamethyltrisiloxane (**17**) and a dimethylsiloxane oligomer of known molecular weight was treated with catalytic amounts of glacial acetic acid and water, and heated to 70 °C with stirring for 120 h, after which the mixture had thickened

visibly. The thick oily product was dissolved in dichloromethane, washed with sodium hydrogencarbonate solution until no further effervescence was observed, dried over anhydrous $MgSO_4$ and filtered. Removal of the volatiles afforded a thick, air stable, colourless oil that was found to be PDMS containing pendant 4-bromobutyl groups.



Reaction data for the two products is presented in **Table 7.1**

Table 7.1: Reaction data for formation of 4-bromobutyl functionalised PDMS

	Siloxane Mw	Ratio Siloxane:HMTSBuBr	Bromobutyl %	Yield %	Mn	Mw/Mn
37	~ 50,000	~ 1.46:1	0.2	84	23,700	3.7
38	~ 25,000	~ 0.58:1	0.5	73	38,550	2.4

^{1}H and ^{29}Si NMR data are presented in **Table 7.2**.

Table 7.2: Selected NMR data for 4-bromobutyl functionalised PDMS

	37	**38**
Si-C*H*$_3$	0.07	0.07
Si-C*H*$_2$-CH$_2$- (m, 2H)	0.40	0.48
Si-CH$_2$-C*H*$_2$- (m, 2H)	1.39	1.37
-C*H*$_2$-CH$_2$Br (m, 2H)	1.88	1.88
-CH$_2$-C*H*$_2$Br (t, 2H)	3.40 (J = 6.7 Hz)	3.39 (J = 6.9 Hz) dt (J = 2.0 Hz)
^{29}Si	-22.0	-22.0

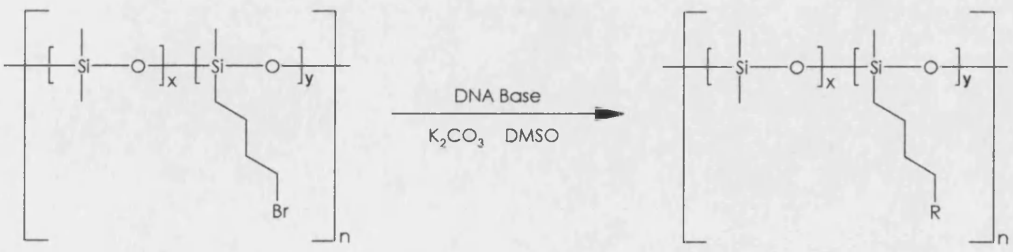
The single peak in the ^{29}Si spectrum at δ = -22.0 ppm, comparing relatively well with the ^{29}Si NMR spectrum of octamethyltrisiloxane [δ = -20.8 ppm],[1] and a lack of peak at ca. δ = 7.5 ppm due to trimethylsiloxy end groups, indicate that **17** has reacted with the siloxane oligomer under acid catalysis to form a homogenous siloxane polymer containing pendant bromobutyl groups. The peaks in the ^{1}H NMR spectrum in both compounds, while of low intensity, were assignable and compare well with those of the trisiloxane starting material **17**.

The number average molecular weights of **37** [23,700] and **38** [38,550] are relatively comparable to those of their siloxane oligomer starting materials [26,550 and 21,950 respectively], and have almost identical polydispersities, suggesting that the inclusion of the bromobutyl group has not significantly altered the length and hydrodynamic volume of the siloxane chain.

7.3 Formation of DNA base functionalised PDMS

Having formed siloxane polymers containing pendant bromobutyl groups in good yield and purity, the next stage was to react them with DNA bases using the same method described in Chapter 5. Thymine and adenine were used, as the two DNA bases that had shown the most consistent results in the formation of compounds modelling the target polymer.

A mixture of potassium carbonate, and the bromobutyl-functionalised PDMS and excess DNA base in question was stirred at room temperature in DMSO for 18 h, after which a white, water soluble precipitate had formed in the reaction mixture. The mixture was filtered and the volatiles removed with under pressure. In each case, the resulting thick, cloudy oil was twice dissolved in chloroform and washed repeatedly with water, before the organic layers were combined and dried over anhydrous magnesium sulphate. Removal of the volatiles afforded very thick, air stable, colourless oils found to be PDMS containing the pendant DNA base *via* a butyl linkage.



Pertinent reaction data for the four compounds are presented in **Table 7.3**.

Table 7.3: Reaction data for formation of DNA functionalised PDMS

	DNA Base	Bromobutyl PDMS	Mn	Mw/Mn	Yield (%)
39	Thymine	**37**	22,100	4.1	55
40	Thymine	**38**	19,050	2.9	43
41	Adenine	**37**	21,250	5.6	48
42	Adenine	**38**	23,600	4.5	41

The ^{1}H and ^{29}Si NMR spectra for the four compounds are presented in **Tables 7.4** and **7.5**.

Table 7.4: Selected NMR data for (4-thymine)butyl PDMS

	39	**40**
Si-C*H*$_3$	0.07	0.07
Si-C*H*$_2$-CH$_2$- (m, 2H)	0.88	0.88
Si-CH$_2$-C*H*$_2$- (m, 2H)	1.39	1.37
-C*H*$_2$-CH$_2$N^1 (m, 2H)	1.70	1.69
-CH$_2$-C*H*$_2$N^1 (m, 2H)	3.70	3.68
C$_{ty}$-*H*	6.97	6.92
C$_{ty}$-C*H*$_3$	1.92	1.92
^{29}Si	-22.0	-22.0

The peaks due to the methylene protons α to the nitrogen in the ^{1}H NMR spectra of **39** and **40** compared with the analogous peaks in the starting materials **37** and **38** suggest a change in the environment of the protons to a more deshielded environment, as would be expected if the CH_2Br group had substituted with the secondary amine. Additionally, all of the peaks due to the alkyl moiety and thymine group in the ^{1}H NMR spectra of **39** and **40** compare very favourably with the analogous peaks in the ^{1}H NMR spectrum of **23**, a strong similarity in the pendant groups of model compound and polymer. These data indicate that the same reaction has taken place as between bromoalkyl functionalised siloxanes and thymine (Chapter 5), and the relative integrals of the peaks due to the methylene protons and the siloxane methyl protons suggest the formation of a siloxane polymer of comparable molecular weight to the starting material. The bromide has substituted exclusively with the most basic 1-position,[2] assigned by comparison with the peaks due to N^1 and N^3 addition in the ^{1}H NMR spectrum of 3-(1-butylthymine)heptamethyltrisiloxane (**23**) and its isomer (**23a**) [δ_{CH2N1} =

3.68 ppm, δ_{CH2N3} = 3.91 ppm]. The ^{29}Si spectra of **39** and **40** compare favourably with that of octamethyltrisiloxane [δ = -20.8 ppm].[1]

The number average molecular weights of **39** [22,100] and **40** [19,050] relative to the starting materials [23,700 and 38,550 respectively] indicate that in the case of the 0.2 % functionalised polymer, the addition of thymine to the siloxane chain has not significantly altered the structure in solution (**Fig.7.1**). However, in the case of the 0.5 % functionalised polymer, the addition of thymine has caused a decrease in the solvated size of the polymer by approximately a half (**Fig.7.2**). This may be due to hydrogen bonding interactions between the pendant thymine molecules in the chain, leading to a smaller excluded volume.

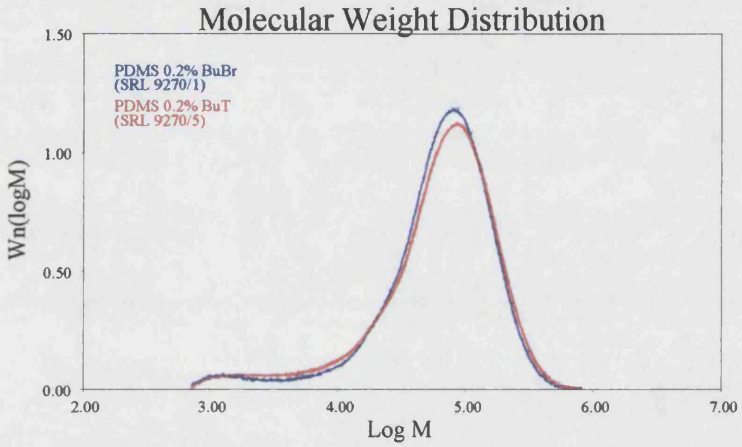


Fig.7.1 Molecular weight distributions of 37 (Blue) and 39 (Red)

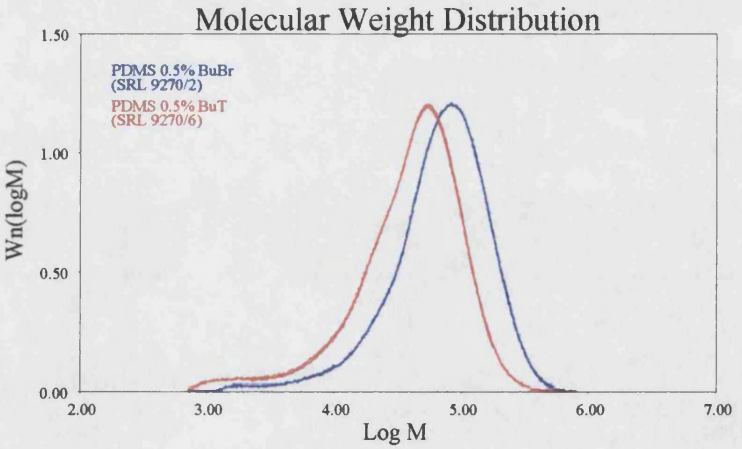


Fig.7.2 Molecular weight distributions of 38 (Blue) and 40 (Red)

Table 7.5: Selected NMR data for (4-adenine)butyl PDMS

	41	**42**
Si-C*H*$_3$	0.08	0.07
Si-C*H*$_2$-CH$_2$- (m, 2H)	0.88	0.88
Si-CH$_2$-C*H*$_2$- (m, 2H)	1.34	1.38
-C*H*$_2$-CH$_2$N^9 (m, 2H)	1.70	1.72
-CH$_2$-C*H*$_2$N^9 (t, 2H)	4.11 (J = 6.0 Hz)	4.14 (J = 6.0 Hz)
C$_{ad}$-*H*	6.96	Not Observed
C$_{ad}$-*H*	6.91	Not Observed
N*H*$_2$	8.02	Not Observed
^{29}Si	-22.0	-22.0

Again, the peaks due to the methylene protons δ to silicon in the ^{1}H NMR spectra shifting downfield relative to the starting materials, and the relatively favourable comparison in peak positions between the spectra **41** and **42** and those in the spectra of the analogous model compound 3-(1-butyladenine)heptamethyltrisiloxane (**26**), indicate a similarity between model compound and polymer and that the reaction has taken place in the same manner as the substitution of bromoalkyl siloxanes with adenine (Chapter 5), with substitution taking place at the most basic 9-position,[2] assigned by comparison of the position of the N^9-C*H*$_2$ peak in the ^{1}H NMR spectrum of **41** and **42** with that in the spectrum of **26**.

The number average molecular weights of **41** [21,250] and **42** [23,600], compared with those of the starting materials [23,700 and 38,550 respectively], indicate a different impact of adding the DNA to the structure of the polymer as with the thymine-functionalised polymers. The molecular weight of the 0.2 % functionalised polymer is not significantly changed in solution by the addition of the adenine to the structure (**Fig.7.3**). However, the addition of adenine to the 0.5 % functionalised polymer has caused a slight increase in molecular weight, possibly due to the size of the adenine molecules holding the chains further apart and leading to a larger solvated volume. This is in direct contrast with that of the thymine functionalised polymers, and further work is of interest to investigate the interactions.

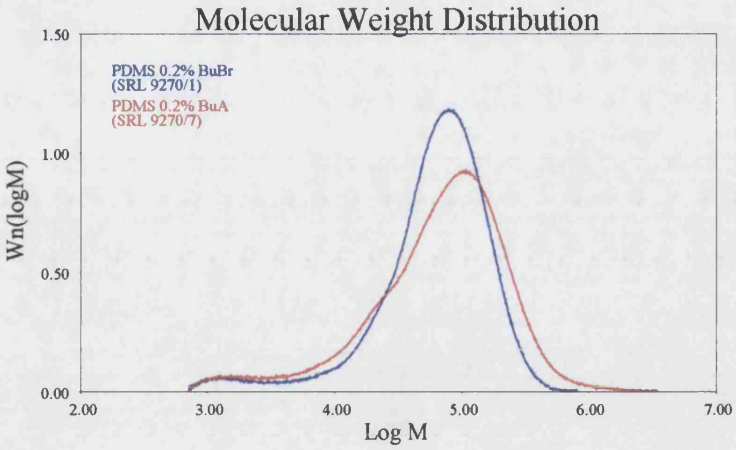


Fig.7.3 Molecular weight distributions of 37 (Blue) and 41 (Red)

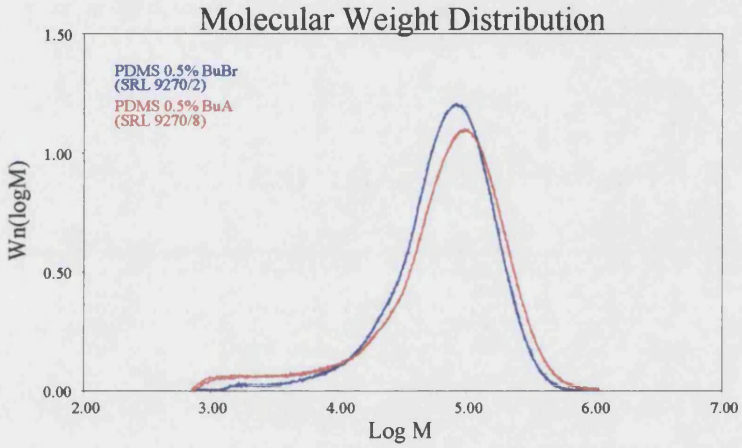


Fig.7.4 Molecular weight distributions of 38 (Blue) and 42 (Red)

In an attempt to investigate the potential solution interactions of the polymer chains *via* hydrogen bonding, equal amounts of the 0.2 % functionalised polymers **39** and **41** were mixed and analysed by ^{1}H NMR. Shifts in the N^{3}-*H* peak in thymine, and in the N*H*$_2$ and C-*H* peaks in adenine, would indicate that hydrogen bonding between the two DNA bases was taking place, forming base pairs *via* one or more of the patterns discussed in Chapter 1, while an increase in Mn by GPC would be expected. Unfortunately, the ^{1}H NMR spectrum of the mixture displays identical peaks due to the potential bonding hydrogens as found in the spectra of pure **39** and **41**, indicating no such interactions are taking place. Furthermore, the molecular weight dispersion trace in the gel permeation chromatogram corresponds to a simple mixture of **39** and **41** (**Fig 7.5**). This suggests no hydrogen bonding interaction takes place in solution between the thymine and adenine functionalised siloxane polymers, bearing

similarities with previous work into the hydrogen bonding interactions of polymer chains containing DNA bases, in which it is observed that higher concentrations of DNA base pairings are required for significant intermolecular interactions to be observed than are present in the functionalised polymers described here.[3]

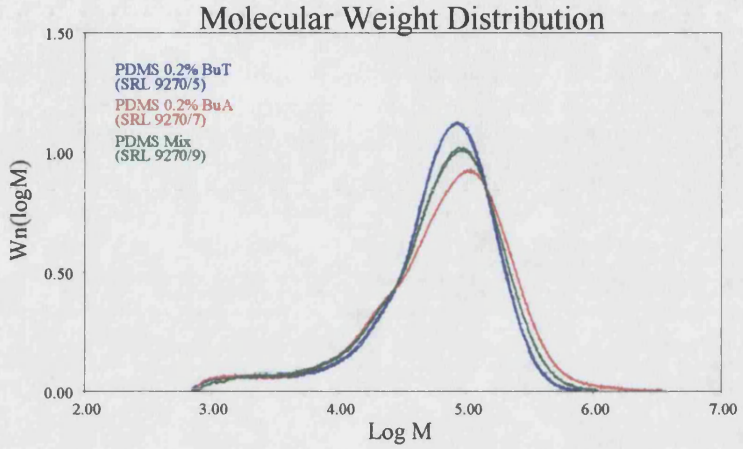


Fig.7.5 Molecular weight distributions of 39 (Blue), 41 (Red), and a mixture thereof (Green)

While polymers produced do not incorporate the concentrations of DNA base originally intended at the start of the investigation, it has been demonstrated that the method employed in their synthesis is viable and potentially extendable. Using the same method as described in this chapter and Chapter 5, the potential exists to synthesise a range of siloxane polymers with higher concentrations of bromobutyl functionality, and in turn to manufacture a wider range of siloxane polymers containing similarly higher concentrations of pendant DNA bases. In high enough concentrations of functionality, conditions may become favourable for measurable intermolecular interactions between the polymer chains to be observed.

7.4 Conclusions

A range of siloxane polymers have been synthesised containing thymine and adenine in known concentration, though the concentration of base is low. Samples of PDMS containing 0.2 % (**37**) and 0.5 % (**38**) bromobutyl functionality have been synthesised, and reacted with thymine and adenine to form siloxane polymers containing 0.2 % pendant thymine (**39**), 0.5 % pendant thymine (**40**), 0.2 % pendant adenine (**41**) and 0.5 % pendant adenine (**42**) functionality, in good yields and acceptable purity.

7.5 Experimental

7.2 Formation of bromobutyl functionalised PDMS

A mixture of 3-(4-bromo)butylheptamethyltrisiloxane (**17**) and a dimethylsiloxane oligomer of known molecular weight was treated with catalytic amounts of glacial acetic acid and water, and stirred at 70 °C for 120 h, after which the mixture had thickened visibly.

Reaction amounts and yields are presented in **Table 7.6**.

Table 7.6: Reactant amounts and yields for bromobutyl siloxane polymers

		Siloxane Oligomer		17				
	Siloxane Mw	g	mmol	g	mmol	**Yield (%)**	**Mn**	**Mw/Mn**
37	~ 50,000	20.4	0.39	0.1	0.28	84	23,700	3.7
38	~ 25,000	4.1	0.16	0.1	0.28	73	38,550	2.4

The thick oily product was dissolved in dichloromethane, washed with sodium hydrogencarbonate solution until no further effervescence was observed, dried over anhydrous $MgSO_4$ and filtered. Removal of the volatiles afforded a thick, air stable, colourless oil that was found to be PDMS containing pendant 4-bromobutyl groups.

PDMS (0.2 % bromobutyl) (**37**): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.40 (t, J = 6.7 Hz, 2H, CH_2Br), 1.88 (m, 2H, CH_2CH_2Br), 1.39 (m, 2H, $SiCH_2CH_2$), 0.40 (m, 2H, $SiCH_2$), 0.07 (s, $SiCH_3$); ^{29}Si NMR (60 MHz, $CDCl_3$): -22.0; GPC: Mn 23,700, Mw/Mn 3.7.

PDMA (0.5 % bromobutyl) (**38**): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.39 (dt, ^{1}J = 6.7 Hz, ^{2}J = 2.0 Hz, 2H, CH_2Br), 1.88 (m, 2H, CH_2CH_2Br), 1.37 (m, 2H, $SiCH_2CH_2$), 0.48 (m, 2H, $SiCH_2$), 0.07 (s, $SiCH_3$); ^{29}Si NMR (60 MHz, $CDCl_3$): -22.0; GPC: Mn 38,550, Mw/Mn 2.4.

7.3 Formation of DNA base functionalised PDMS

A mixture of potassium carbonate, and the bromobutyl-functionalised PDMS and excess DNA base in question was stirred at room temperature in DMSO ($50cm^3$) for 18 h, after which a white, water soluble precipitate had formed in the reaction mixture.

Reaction amounts and yields are presented in **Table 7.6** and **7.7**.

Table 7.6: Reactant amounts and yields for thymine functionalised PDMS

	BuBr conc (%)	Polymer		Thymine		K_2CO_3		Yield (%)	Mn	Mw/Mn
		g	mmol	g	mmol	g	mmol			
39	0.2	1.0	0.02	0.05	0.35	0.05	0.35	55	22,100	4.1
40	0.5	1.0	0.07	0.01	0.07	0.01	0.07	43	19,050	2.9

Table 7.7: Reactant amounts and yields for adenine functionalised PDMS

	BuBr conc (%)	Polymer		Adenine		K_2CO_3		Yield (%)	Mn	Mw/Mn
		g	mmol	g	mmol	g	mmol			
39	0.2	1.0	0.02	0.05	0.35	0.05	0.35	48	21,250	5.6
40	0.5	1.8	0.12	0.29	2.13	0.29	2.13	41	23,600	4.5

The mixture was filtered and the volatiles removed with under pressure. In each case, the resulting thick, cloudy oil was twice dissolved in chloroform and washed repeatedly with water, before the organic layers were combined and dried over anhydrous magnesium sulphate. Removal of the volatiles afforded very thick, air stable, colourless oils found to be PDMS containing the pendant DNA base *via* a butyl linkage.

PDMS (0.2 % butylthymine) (**39**): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.97 (s, 1H, $C_{ty}H$), 3.70 (m, 2H, CH_2N^1), 1.92 (s, 3H, $C_{ty}CH_3$), 1.70 (m, 2H, $CH_2CH_2N^1$), 1.39 (m, 2H, $SiCH_2CH_2$), 0.88 (m, 2H, $SiCH_2$), 0.07 (s, $SiCH_3$); ^{29}Si NMR (60 MHz, $CDCl_3$): δ = -22.0; GPC: Mn 21,250, Mw/Mn 4.1.

PDMS (0.5 % butylthymine) (**40**): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.92 (s, 1H, $C_{ty}H$), 3.68 (m, 2H, CH_2N^1), 1.92 (s, 3H, $C_{ty}CH_3$), 1.69 (m, 2H, $CH_2CH_2N^1$), 1.37 (m, 2H, $SiCH_2CH_2$), 0.88 (m, 2H, $SiCH_2$), 0.07 (s, $SiCH_3$); ^{29}Si NMR (60 MHz, $CDCl_3$): δ = -22.0; GPC: Mn 19,050, Mw/Mn 2.9.

PDMS (0.2 % butyladenine) (**41**): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.02 (bs, 2H, NH_2), 6.96 (s, 1H, $C_{ad}H$), 6.91 (s, 1H, $C_{ad}H$), 4.11 (t, J = 6.0 Hz, 2H, CH_2N^9), 1.70 (m, 2H, $CH_2CH_2N^9$), 1.34 (m, 2H, $SiCH_2CH_2$), 0.88 (m, 2H, $SiCH_2$), 0.07 (s, $SiCH_3$); ^{29}Si NMR (60 MHz, $CDCl_3$): δ = -22.0; GPC: Mn 21,250, Mw/Mn 5.6.

PDMS (0.5% butyladenine) (**42**): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.14 (t, J = 6.0 Hz, 2H, CH_2N^9), 1.72 (m, 2H, $CH_2CH_2N^9$), 1.38 (m, 2H, $SiCH_2CH_2$), 0.88 (m, 2H, $SiCH_2$), 0.07 (s, $SiCH_3$); ^{29}Si NMR (60 MHz, $CDCl_3$): δ = -22.0; GPC: Mn 23,600, Mw/Mn 4.5.

7.6 References

1 P. Lux, F. Brunet, H. Desvaux, and J. Virlet, *Magn. Reson. Chem.*, 1993, **31**, 623.
2 B. Lippert, *Coord. Chem. Rev.*, 2000, **200-202**, 487.
3 K. C. Schneider and S. A. Benner, *J. Am. Chem. Soc.*, 1990, **112**, 453.

Chapter 8

Appendices

8.1 Appendix I – Experimental Procedures

Starting materials adenine, thymine, cytosine, guanine, phenyldimethylsilane, (3-aminopropyl)-diethoxymethylsilane, chlorodimethylsilane, chloroplatinic acid, allylamine, allyl bromide, 4-bromo-1-butene, hexamethyldisilazane, *p*-tolualdehyde, 3-bis-(3-aminopropyl)tetramethyldisiloxane, PDMS (Mw ~ 50,000) and PDMS (Mw ~ 25,000) were obtained from Sigma-Aldrich and used without further purification. Pentamethyldisiloxane and 1,1,1,3,5,5,5-heptamethyltrisiloxane were obtained from Gelest. All reactions were carried out under nitrogen unless otherwise specified.

Infra-red spectra were recorded as liquid films on NaCl plates using a Nexus Nicolet 510P FT-IR spectrometer in the region 4000-400 cm^{-1}.

^{1}H, ^{13}C and ^{29}Si spectra were recorded on Bruker Avance (300 MHz) Fourier transform spectrometer, using TMS as an internal reference.

Elemental analyses were performed using a Carbo Erba Strumentazione E.A. mod 1106 analyser. The results were duplicated and the mean of the duplicated measurements was the final result.

X-Ray crystallography was carried out on an Enraf-Nonius CAD-4 diffractometer, and the data was collected for **1**, **2**, **3**, **4**, **8**, **9**, **10**, **11**, **12**, **19**, **21**, **28** and **30**. The atomic coordinates and equivalent isotropic displacement parameters of these compounds is available as supplementary data. For all the compounds, data were corrected for both extinction and absorption effects; hydrogens were added at calculated positions. The asymmetric unit along with the labelling scheme used was produced using X-Seed.[1]

8.2 Appendix II - Crystallographic analysis and structural refinement of bis-(trimethylsilyl)thymine (1)

Identification code	h04kcm30
Empirical formula	$C_{11}H_{22}N_2O_2Si_2$
Formula weight	270.49
Temperature	150(2) K
Wavelength	0.71073 Å
Crystal system	Tetragonal
Space group	$P\,4_3\,4_2\,2$
Unit cell dimensions	a = 11.09200(10) Å $\alpha = 90°$
	b = 11.09200(10) Å $\beta = 90°$
	c = 25.5720(4) Å $\gamma = 90°$
Volume	3146.19(6) $Å^3$
Z	8
Density (calculated)	1.142 Mg/m^3
Absorption coefficient	0.220 mm^{-1}
F(000)	1168
Crystal size	0.45 x 0.10 x 0.08 mm
Theta range for data collection	3.05 to 27.37°
Index ranges	$-13 \le h \le 13$; $-11 \le k \le 13$; $-31 \le l \le 30$
Reflections collected	21526
Independent reflections	3123 [R(int) = 0.0637]
Data Completeness	0.993
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3213 / 0 / 160
Goodness-of-fit on F^2	1.100
Final R indices [$I>2\sigma(I)$]	$R_1 = 0.0377$ $wR_2 = 0.0974$
R indices (all data)	$R_1 = 0.0448$ $wR_2 = 0.1006$
Absolute structure parameter	0.04(14)
Largest diff. peak and hole	0.442 and -0.427 $eÅ^{-3}$

8.3 Appendix III - Crystallographic analysis and structural refinement of bis-(trimethylsilyl)cytosine (2)

Identification code	h04kcm1
Empirical formula	$C_{10} H_{21} N_3 O Si_2$
Formula weight	255.48
Temperature	150(2) K
Wavelength	0.71073 Å
Crystal system	Orthorhombic
Space group	$P 2_1 2_1 2_1$
Unit cell dimensions	$a = 11.7150(3)$ Å $\alpha = 90°$
	$b = 11.8760(3)$ Å $\beta = 90°$
	$c = 21.7350(7)$ Å $\gamma = 90°$
Volume	3023.93(15) $Å^3$
Z	8
Density (calculated)	1.122 Mg/m^3
Absorption coefficient	0.222 mm^{-1}
F(000)	1104
Crystal size	0.35 x 0.15 x 0.08 mm
Theta range for data collection	3.73 to 27.62°
Index ranges	$-15 \leq h \leq 13$; $-13 \leq k \leq 15$; $-27 \leq l \leq 21$
Reflections collected	19385
Independent reflections	6694 [R(int) = 0.0789]
Reflections observed (I>2 σ)	4810
Data Completeness	0.966
Absorption correction	None
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	6694 / 2 / 310
Goodness-of-fit on F^2	1.092
Final R indices [I>2σ(I)]	$R_1 = 0.0456$ $wR_2 = 0.0824$
R indices (all data)	$R_1 = 0.0880$ $wR_2 = 0.1070$
Absolute structure parameter	-0.10(13)
Largest diff. peak and hole	0.274 and -0.424 $eÅ^{-3}$

8.4 Appendix IV - Crystallographic analysis and structural refinement of bis-(trimethylsilyl)adenine (3)

Identification code	h04kcm28
Empirical formula	C_{11} H_{21} N_5 Si_2
Formula weight	279.51
Temperature	150(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	C 2/c
Unit cell dimensions	a = 23.1570(7) Å α = 90°
	b = 12.2300(4) Å β = 97.794(2)°
	c = 22.9030(8) Å γ = 90°
Volume	6426.4(4) $Å^3$
Z	16
Density (calculated)	1.156 Mg/m^3
Absorption coefficient	0.214 mm^{-1}
F(000)	2400
Crystal size	0.28 x 0.28 x 0.10 mm
Theta range for data collection	3.76 to 27.60°
Index ranges	$-30 \leq h \leq 29$; $-15 \leq k \leq 15$; $-29 \leq l \leq 29$
Reflections collected	46330
Independent reflections	7313 [R(int) = 0.0985]
Data Completeness	0.983
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	7313 / 0 / 345
Goodness-of-fit on F^2	1.025
Final R indices [$I>2\sigma(I)$]	R_1 = 0.0580 wR_2 = 0.1434
R indices (all data)	R_1 = 0.1161 wR_2 = 0.1666
Largest diff. peak and hole	1.030 and -0.437 $eÅ^{-3}$

8.5 Appendix V - Crystallographic analysis and structural refinement of tris-(trimethylsilyl)guanine (4)

Identification code	h04kcm24
Empirical formula	$C_{14}H_{29}N_5OSi_3$
Formula weight	367.69
Temperature	150(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	$P\ 2_1/n$
Unit cell dimensions	$a = 17.1050(5)$ Å $\alpha = 90°$
	$b = 6.8600(2)$ Å $\beta = 112.662(2)°$
	$c = 20.3940(7)$ Å $\gamma = 90°$
Volume	2208.28(12) $Å^3$
Z	4
Density (calculated)	1.106 Mg/m^3
Absorption coefficient	0.225 mm^{-1}
F(000)	792
Crystal size	0.75 x 0.40 x 0.32 mm
Theta range for data collection	5.95 to 25.00°
Index ranges	$-20 \leq h \leq 20$; $-8 \leq k \leq 8$; $-24 \leq l \leq 23$
Reflections collected	22773
Independent reflections	3761 [R(int) = 0.0970]
Data Completeness	0.967
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2761 / 0 / 221
Goodness-of-fit on F^2	1.087
Final R indices [$I>2\sigma(I)$]	$R_1 = 0.0837$ $wR_2 = 0.1866$
R indices (all data)	$R_1 = 0.1112$ $wR_2 = 0.2146$
Largest diff. peak and hole	0.542 and -0.305 $eÅ^{-3}$

8.6 Appendix VI - Crystallographic analysis and structural refinement of bis-1,3-bisallylcytosinium bromide (8)

Identification code	h06kcm3
Empirical formula	$C_{10}H_{14}BrN_3O$
Formula weight	272.15
Temperature	150(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	P 1
Unit cell dimensions	a = 5.1210(6) Å α = 96.622(5)°
	b = 8.8530(10) Å β = 99.094(8)°
	c = 13.6040(13) Å γ = 99.440(4)°
Volume	594.40(12) $Å^3$
Z	2
Density (calculated)	1.521 Mg/m^3
Absorption coefficient	3.437 mm^{-1}
F(000)	276
Crystal size	0.50 x 0.10 x 0.03 mm
Theta range for data collection	2.99 to 27.63°
Index ranges	$-6\leq h\leq 6$; $-11\leq k\leq 11$; $-16\leq l\leq 17$
Reflections collected	6288
Independent reflections	2686 [R(int) = 0.0995]
Data Completeness	0.970
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2686 / 0 / 136
Goodness-of-fit on F^2	0.981
Final R indices [$I>2\sigma(I)$]	$R_1 = 0.0592$ $wR_2 = 0.1362$
R indices (all data)	$R_1 = 0.0985$ $wR_2 = 0.15.43$
Largest diff. peak and hole	0.563 and -0.896 $eÅ^{-3}$

8.7 Appendix VII - Crystallographic analysis and structural refinement of 7,9-bis-(allyl)adeninium bromide hydrate (9)

Identification code	k05kcm21
Empirical formula	$C_{11}\ H_{15.5}\ Br\ N_5\ O_{0.75}$
Formula weight	309.69
Temperature	240(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	P-1
Unit cell dimensions	a = 7.4800(2) Å α = 85.969(1)°
	b = 12.7660(3) Å β = 88.427(1)°
	c = 14.7150(4) Å γ = 88.238(2)°
Volume	1400.54(15) $Å^3$
Z	4
Density (calculated)	1.469 Mg/m^3
Absorption coefficient	2.930 mm^{-1}
F(000)	630
Crystal size	0.10 x 0.05 x 0.05 mm
Theta range for data collection	3.94 to 27.7°
Index ranges	$-9\leq h\leq 9$; $-16\leq k\leq 16$; $-19\leq l\leq 19$
Reflections collected	22780
Independent reflections	6405 [R(int) = 0.0734]
Reflections observed (I>2 σ)	4244
Data Completeness	0.973
Absorption correction	Semi-emprical from equivalents
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	6405 / 4 / 307
Goodness-of-fit on F^2	1.114
Final R indices [I>2σ(I)]	$R_1 = 0.0750$ $wR_2 = 0.1156$
R indices (all data)	$R_1 = 0.1283$ $wR_2 = 0.1286$
Largest diff. peak and hole	0.623 and -0.509 $eÅ^{-3}$

8.8 Appendix VIII - Crystallographic analysis and structural refinement of 4-butenyladeninium bromide (10)

Identification code	h05kcm29
Empirical formula	$C_9 H_{12} Br N_5$
Formula weight	270.15
Temperature	150(2) K
Wavelength	0.71073 Å
Crystal system	Orthorhombic
Space group	P c a b
Unit cell dimensions	a = 11.2010(2) Å α = 90°
	b = 11.4150(2) Å β = 90°
	c = 18.4330(3) Å γ = 90°
Volume	2356.83(7) $Å^3$
Z	8
Density (calculated)	1.523 Mg/m^3
Absorption coefficient	3.465 mm^{-1}
F(000)	1088
Crystal size	0.30 x 0.15 x 0.10 mm
Theta range for data collection	5.26 to 27.51°
Index ranges	$-14 \leq h \leq 14$; $-14 \leq k \leq 14$; $-23 \leq l \leq 22$
Reflections collected	32199
Independent reflections	2680 [R(int) = 0.0631]
Reflections observed (I>2 σ)	2378
Data Completeness	0.990
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2680 / 0 / 136
Goodness-of-fit on F^2	1.168
Final R indices [I>2σ(I)]	$R_1 = 0.0366$ $wR_2 = 0.0937$
R indices (all data)	$R_1 = 0.0422$ $wR_2 = 0.0971$
Largest diff. peak and hole	0.443 and -0.733 $eÅ^{-3}$

8.9 Appendix IX - Crystallographic analysis and structural refinement of (trimethylsilyl)-1-allylthymine (11)

Identification code	h04kcm2
Empirical formula	$C_{11}\ H_{18}\ N_2\ O_2\ Si$
Formula weight	238.36
Temperature	150(2) K
Wavelength	0.71073 Å
Crystal system	Orthorhombic
Space group	$P\ n\ a\ 2_1$
Unit cell dimensions	a = 13.0220(2) Å $\alpha = 90°$
	b = 17.4770(3) Å $\beta = 90°$
	c = 12.0850(2) Å $\gamma = 90°$
Volume	2750.37(8) $Å^3$
Z	8
Density (calculated)	1.151 Mg/m^3
Absorption coefficient	0.161 mm^{-1}
F(000)	1024
Crystal size	0.58 x 0.10 x 0.08 mm
Theta range for data collection	4.92 to 27.48°
Index ranges	$-16 \leq h \leq 16$; $-22 \leq k \leq 22$; $-15 \leq l \leq 15$
Reflections collected	46491
Independent reflections	6222 [R(int) = 0.0792]
Data Completeness	0.991
Absorption correction	None
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	6222 / 1 / 297
Goodness-of-fit on F^2	1.035
Final R indices [$I>2\sigma(I)$]	$R_1 = 0.0382$ $wR_2 = 0.0830$
R indices (all data)	$R_1 = 0.0577$ $wR_2 = 0.0912$
Absolute structure parameter	0.01(9)
Largest diff. peak and hole	0.156 and -0.181 $eÅ^{-3}$

8.10 Appendix X - Crystallographic analysis and structural refinement of (4-phenyldimethylsilyl)butylthymine (12)

Identification code	k04kcm13
Empirical formula	$C_{17}H_{24}N_2O_2Si$
Formula weight	316.47
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	P-1
Unit cell dimensions	a = 8.0960(4) Å α = 98.284(3)°
	b = 8.3770(5) Å β = 92.095(3)°
	c = 13.0730(7) Å γ = 99.840(2)°
Volume	862.75(8) $Å^3$
Z	2
Density (calculated)	1.218 Mg/m^3
Absorption coefficient	0.145 mm^{-1}
F(000)	340
Crystal size	0.30 x 0.40 x 0.05 mm
Theta range for data collection	5.53 to 27.53°
Index ranges	$-10 \leq h \leq 10$; $-10 \leq k \leq 10$; $-16 \leq l \leq 16$
Reflections collected	9597
Independent reflections	3883 [R(int) = 0.0449]
Data Completeness	0.976
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3883 / 0 / 206
Goodness-of-fit on F^2	1.043
Final R indices [$I>2\sigma(I)$]	$R_1 = 0.0465$ $wR_2 = 0.1191$
R indices (all data)	$R_1 = 0.0579$ $wR_2 = 0.1288$
Largest diff. peak and hole	0.305 and -0.383 $eÅ^{-3}$

8.11 Appendix XI - Crystallographic analysis and structural refinement of (4-phenyldimethylsilyl)butylcytosine (19)

Identification code	bath158
Empirical formula	$C_{17}H_{23}N_2OSi$
Formula weight	299.46
Temperature	150(2) K
Wavelength	0.8460 Å
Crystal system	Monoclinic
Space group	P 21/c
Unit cell dimensions	a = 9.5090(15) Å α = 90°
	b = 40.651(6) Å β = 98.108(3)°
	c = 8.7418(13) Å γ = 90°
Volume	3345.3(9) $Å^3$
Z	8
Density (calculated)	1.189 Mg/m^3
Absorption coefficient	0.141 mm^{-1}
F(000)	1288
Crystal size	0.10 x 0.08 x 0.02 mm
Theta range for data collection	4.24 to 33.20°
Index ranges	$-12\leq h\leq 12$; $-50\leq k\leq 49$; $-11\leq l\leq 11$
Reflections collected	24748
Independent reflections	7007 [R(int) = 0.0680]
Reflections observed (I>2 σ)	4252
Data Completeness	0.921
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	7007 / 0 / 383
Goodness-of-fit on F^2	1.060
Final R indices [I>2σ(I)]	$R_1 = 0.0720$ $wR_2 = 0.2107$
R indices (all data)	$R_1 = 0.1121$ $wR_2 = 0.2407$
Largest diff. peak and hole	0.820 and -0.428 $eÅ^{-3}$

8.12 Appendix XII - Crystallographic analysis and structural refinement of 6,6,8,8,15-Pentamethyl-7-oxa-1,13-diaza-6,8-disila-bicyclo[11.3.1]heptadec-15-ene-14,17-dione (21)

Identification code	h06kcm6
Empirical formula	$C_{17}H_{31}N_2O_3Si_2$
Formula weight	367.62
Temperature	150(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	P-1
Unit cell dimensions	a = 7.6870(3) Å α = 85.273(2)°
	b = 8.6440(4) Å β = 79.127(2)°
	c = 17.9510(11) Å γ = 64.283(2)°
Volume	1055.34(9) $Å^3$
Z	2
Density (calculated)	1.157 Mg/m^3
Absorption coefficient	0.184 mm^{-1}
F(000)	398
Crystal size	0.25 x 0.20 x 0.05 mm
Theta range for data collection	5.73 to 25.53°
Index ranges	$-9\leq h\leq 9$; $-10\leq k\leq 10$; $-21\leq l\leq 21$
Reflections collected	11515
Independent reflections	3797 [R(int) = 0.0664]
Reflections observed (I>2 σ)	2589
Data Completeness	0.962
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3797 / 0 / 232
Goodness-of-fit on F^2	1.029
Final R indices [I>2σ(I)]	$R_1 = 0.0595$ $wR_2 = 0.1328$
R indices (all data)	$R_1 = 0.0944$ $wR_2 = 0.1531$
Largest diff. peak and hole	0.269 and -0.343 $eÅ^{-3}$

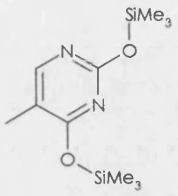
8.13 Appendix XIII - Crystallographic analysis and structural refinement of 16-amino-6,6,8,8-tetramethyl-7-oxa-1,13-diaza-6,8-disila-bicyclo[11.3.1]heptadec-14-en-17-one (28)

Identification code	k06kcm4
Empirical formula	$C_{16}H_{31}N_3O_2Si_2$
Formula weight	353.62
Temperature	150(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	P-1
Unit cell dimensions	a = 7.1750(2)Å α = 96.026(1)°
	b = 8.9310(3)Å β = 96.811(1)°
	c = 15.8080(6)Å γ = 95.330(2)°
Volume	994.56(6) $Å^3$
Z	2
Density (calculated)	1.181 Mg/m^3
Absorption coefficient	0.190 mm^{-1}
F(000)	384
Crystal size	0.25 x 0.25 x 0.10 mm
Theta range for data collection	5.73 to 25.53°
Index ranges	$-9\leq h\leq 9$; $-11\leq k\leq 11$; $-20\leq l\leq 20$
Reflections collected	15781
Independent reflections	4533 [R(int) = 0.0447]
Reflections observed (I>2 σ)	3724
Data Completeness	0.988
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4533 / 0 / 255
Goodness-of-fit on F^2	1.131
Final R indices [I>2σ(I)]	$R_1 = 0.0556$ $wR_2 = 0.1173$
R indices (all data)	$R_1 = 0.0757$ $wR_2 = 0.1240$
Largest diff. peak and hole	0.344 and -0.541 $eÅ^{-3}$

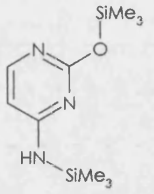
8.14 Appendix XIV - Crystallographic analysis and structural refinement of 4-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-ylmethyl)benzaldehyde (30)

Identification code	k05kcm4
Empirical formula	$C_{13}\ H_{12}\ N_2\ O_3$
Formula weight	244.25
Temperature	150(2) K
Wavelength	0.71073 Å
Crystal system	Monclinic
Space group	P 21/n
Unit cell dimensions	a = 4.64000(10) Å $\alpha = 90^\circ$
	b = 11.7910(3) Å $\beta = 96.0310(10)^\circ$
	c = 21.2560(5) Å $\gamma = 90^\circ$
Volume	1156.48(5) $Å^3$
Z	4
Density (calculated)	1.403 Mg/m^3
Absorption coefficient	0.102 mm^{-1}
F(000)	512
Theta range for data collection	3.37 to 24.92°
Index ranges	$-5 \leq h \leq 5$; $-13 \leq k \leq 13$; $-25 \leq l \leq 25$
Reflections collected	16174
Independent reflections	2008 [R(int) = 0.0463]
Reflections observed (I>2 σ)	1774
Data Completeness	0.993
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2008 / 0 / 169
Goodness-of-fit on F^2	1.082
Final R indices [I>2σ(I)]	$R_1 = 0.0424$ $wR_2 = 0.1090$
R indices (all data)	$R_1 = 0.0578$ $wR_2 = 0.1146$
Largest diff. peak and hole	0.472 and -0.295 $eÅ^{-3}$

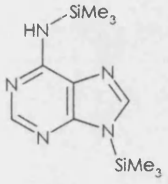
8.15 Numerical list of compounds



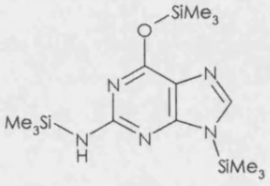
1. bis-(trimethylsilyl)thymine



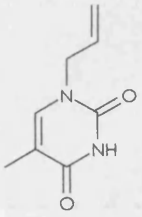
2. bis-(trimethylsilyl)cytosine



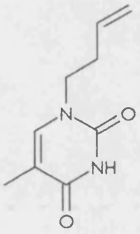
3. bis-(trimethylsilyl)adenine



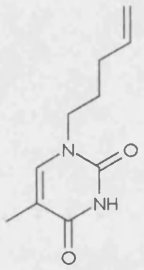
4. tris-(trimethylsilyl)guanine



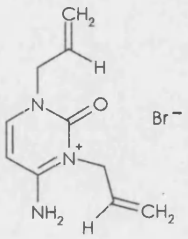
5. 1-allylthymine



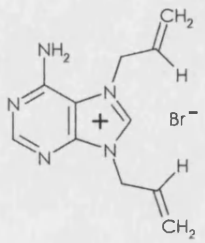
6. 1-butenylthymine



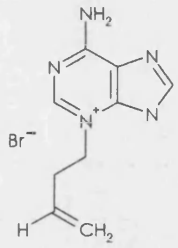
7. 1-pentenylthymine



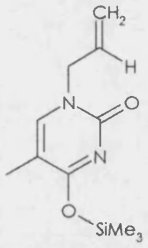
8. 1,3-bisallylcytosinium bromide



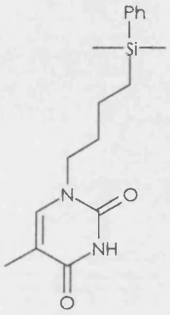
9. 7,9-bisallyladeninium bromide



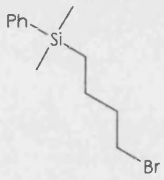
10. 3-butenyladenenium bromide



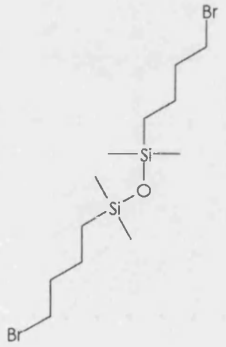
11. trimethylsilyl-1-allylthymine



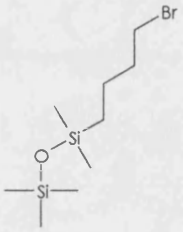
12. (4-phenyldimethylsilyl)butylthymine



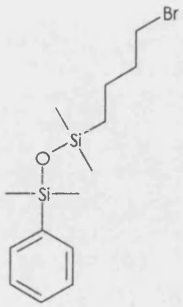
13. 4-(phenyldimethylsilyl)-1-bromobutane



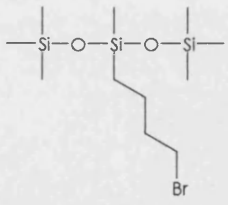
14. 1,3-bis(4-bromobutyl)tetramethyldisiloxane



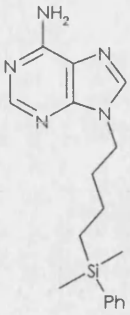
15. 4-bromobutylpentamethyldisiloxane



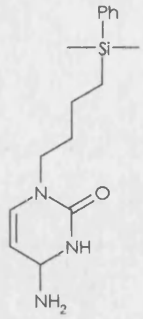
16. 1-(4-bromobutyl)-3-phenyltetramethyldisiloxane



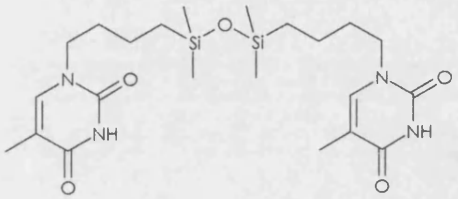
17. 3-(4-bromo)butylheptamethyltrisiloxane



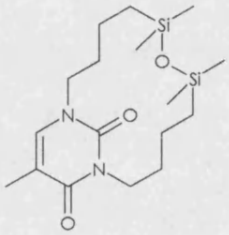
18. (4-phenyldimethylsilyl)butyladenine



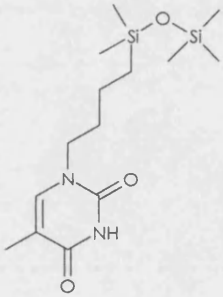
19. (4-phenyldimethylsilyl)butylcytosine



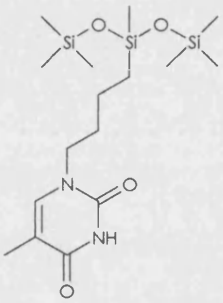
20. 1,3-bis(1-butylthymine)tetramethyldisiloxane



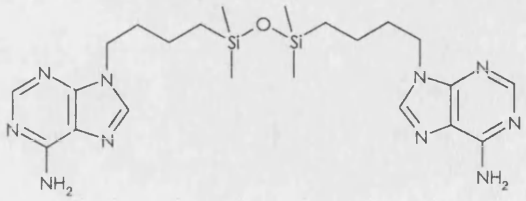
21. 6,6,8,8,15-Pentamethyl-7-oxa-1,13-diaza-6,8-disila-bicyclo[11.3.1]heptadec-15-ene-14,17-dione



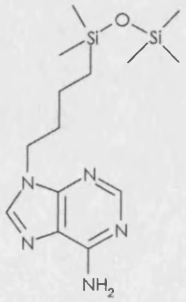
22. 4-pentamethyldisiloxy-1-butylthymine



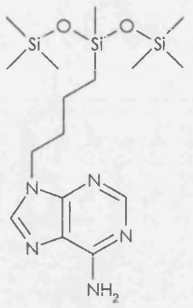
23. 3-(1-butylthymine)heptamethyltrisiloxane



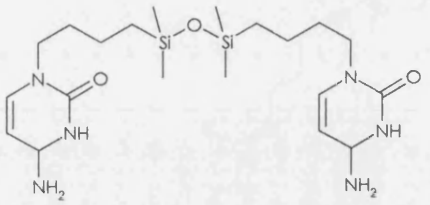
24. 1,3-bis(9-butyladenine)tetramethyldisiloxane



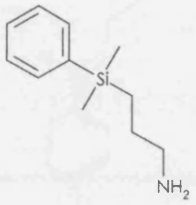
25. 4-pentamethyldisiloxy-9-butyladenine



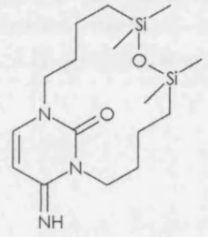
26. 3-(9-butyladenine)heptamethyltrisiloxane



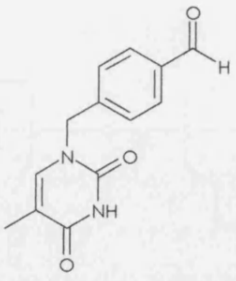
27. 1,3-bis(1-butylcytosine)tetramethyldisiloxane



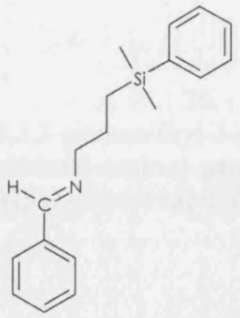
29. (3-aminopropyl)phenyldimethylsilane



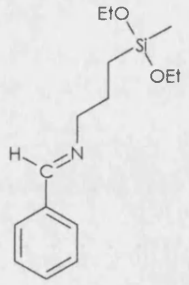
28.
16-Amino-6,6,8,8-tetramethyl-7-oxa-1,13-diaza-6,8-disila-bicyclo[11.3.1]heptadec-14-en-17-one



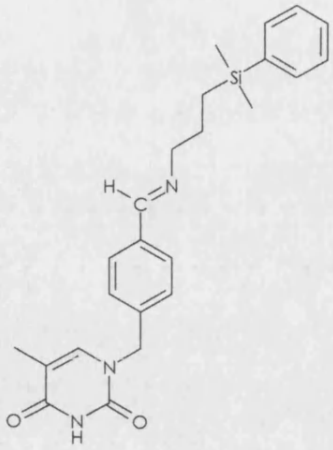
30.
4-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-ylmethyl)benzaldehyde



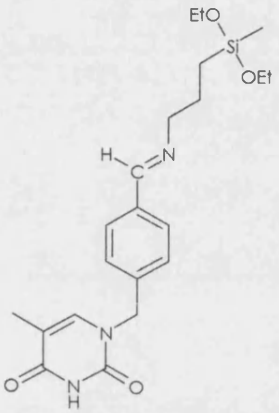
31.
[3-(Dimethyl-phenyl-silanyl)-propyl]-[1-phenyl-meth-(E)-ylidene]-amine



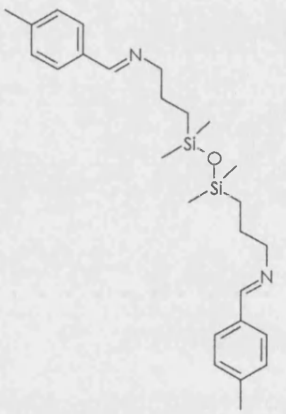
32.
[3-(Diethoxy-methyl-silanyl)-propyl]-[1-phenyl-meth-(E)-ylidene]-amine



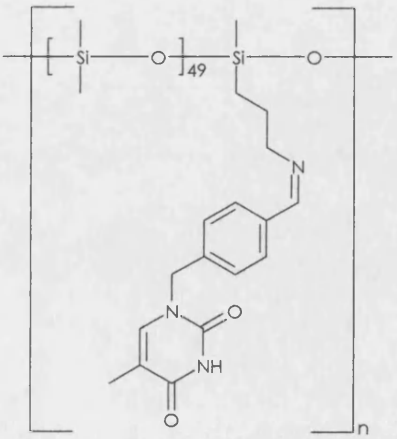
33.
1-(4-{[(E)-3-(Dimethyl-phenyl-silanyl)-propylimino]-methyl}-benzyl)-5-methyl-1*H*-pyrimidine-2,4-dione



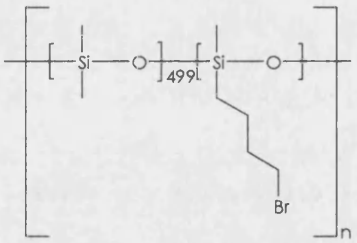
34.
1-(4-{[(E)-3-(Diethoxy-methyl-silanyl)-propylimino]-methyl}-benzyl)-5-methyl-1*H*-pyrimidine-2,4-dione



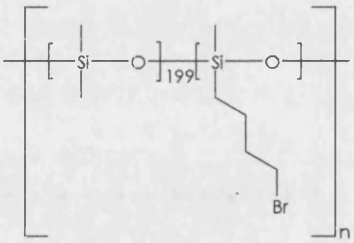
35.
{3-[1,1,3,3-tetramethyl-3-(3-{[1-*p*-tolyl-meth-(E)-ylidene]-amino}-propyl)-disiloxanyl]-propyl}-[1-*p*-tolyl-meth-(E)-ylidene]-amine



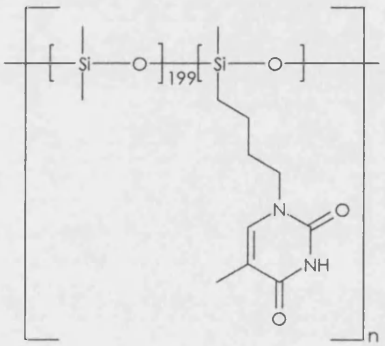
36. PDMS (2 % propyl-imino-1-benzylthymine)



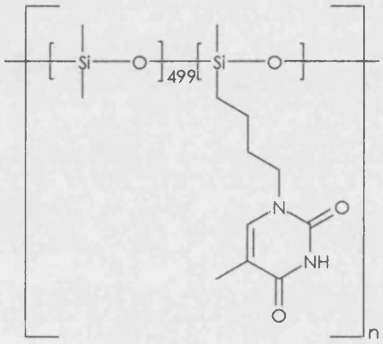
37. PDMS (0.2 % bromobutyl)



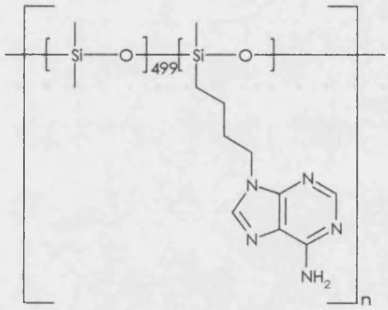
38. PDMS (0.5 % bromobutyl)



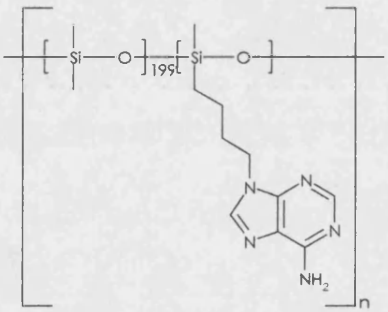
39. PDMS (0.2 % butylthymine)



40. PDMS (0.5 % butylthymine)



41. PDMS (0.2 % butyladenine)



42. PDMS (0.5 % butyladenine)

8.16 References

1 J. Barbour, *J. Supramol. Chem.*, 2001, **1**, 189.